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VARIATION IN THE CHOLESTEROL, BILE PIGMENT AND CALCIUM SALTS CONTENTS OF GALLSTONES FORMED IN GALLBLADDER AND IN BILE DUCTS WITH THE DEGREE OF ASSOCIATED OBSTRUCTION *

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THE fundamental cause of gallstone formation is still very little understood despite the amount of study which has been devoted to the physiology and chemistry of the bile, the composition of the stones, and the associated pathology and bacteriology of the biliary tract. Stones may form either in the gallbladder or in the bile ducts, and both sites have to be considered in determining the rôle which any factor may play in determining their chemical composition. This fact is often lost sight of and proportionately much more attention has been paid to stone formation in the gallbladder than to that in the bile ducts. Some of the factors that have been considered, or are known to influence stone formation, are obstruction, infection, reflux of pancreatic juice or duodenal contents, altered cholesterol metabolism with increased output of cholesterol in the bile, increased bile pigment output in hemolytic icterus, reduction in the ratio between nonsaponifiable substances (cholesterol) and saponifiable substances (fats and fatty acids) in the bile, dyskinesis, and overconcentration of the salts of the bile acids with resultant injury to the gallbladder wall. Of these, the one whose rôle is most clearly established, although it may not be of fundamental importance, is obstruction.

Clinical and operative studies have been made of cases of cholelithiasis and traumatic strictures of the ducts, and chemical analyses, radiograms, and roentgenographic powder diagrams have been made of stones removed from such gallbladders and common and hepatic ducts, in an endeavor to throw light on their chemical composition as influenced by the site of stone formation and by any coexisting obstruction; also on the source of the chemicals themselves, whether they are derived from the bile or from the wall of the gallbladder.

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CHEMICAL METHODS.—Cholesterol was determined by the method of Bloor, Pelkan and Allen[1] for blood cholesterol applied to an ether extract of the stones. Calcium was determined by the method of Clark and Collip,[2] and phosphorus by the method of Phiske and Subbarrow.[3] Bile pigments were determined by a method introduced by one of us (H. G. A.[4]) as follows: The stones were extracted with a mixture of equal parts of chloroform, alcohol and glacial acetic acid. The extract was refluxed and then oxydized to a blue end-point with perchloric acid. Standard bilirubin solution was used for comparison.

PHYSICAL METHOD.—Roentgenographic powder diagrams were made of the stones in the following way: The material, first unpowdered and then powdered, was placed in a Pyrex tube which in turn was placed in a cylindrical powder camera and radiated by roentgen rays (copper K alpha) for ten hours. The resulting lines on the exposed films serve to identify the materials. This analysis is capable of indicating not only certain chemical compounds but also the specific crystalline forms in which they may be present. Detailed reports of the analyses are given in a separate publication by one of us (R. P.[5]).

Stones Formed in the Gallbladder.—The chief building materials of stones in the gallbladder are cholesterol, bile pigments and calcium compounds, predominantly calcium carbonate; but in two cases the compound of tricalcium phosphate and calcium carbonate, resembling dahlite, was present. The materials become enmeshed in a colloidal ground substance as is common to all concrement formation. They may be present in greatly variable amounts and in nearly all possible combinations. Pure cholesterol stones usually develop singly in the gallbladder. Since the work of Aschoff[6] and his collaborators, it has been generally accepted that they arise from stasis in the absence of infection, but in patients with altered cholesterol metabolism. Since they so frequently develop in connection with pregnancy, the finding of increased cholesterol in the bile, aspirated from the gallbladder during cesarean section, by Riegal, Ravdin and Morrison,[7] Boyden and Potter,[8] and at autopsy by MacNee,[9] lends support to the theory of stasis and altered cholesterol metabolism. Pure cholesterol stones, especially solitary stones, may be found in gallbladders showing no pathologic change, and cholecystography shows visualization by the dye in a high percentage of cases before complications have arisen (Graham[10]). The latter finding is evidence that cholesterol stones form in the presence of a relatively small amount of obstruction.

In contrast with these findings, pure calcium carbonate is known to be laid down in gallbladders, the seat of mild, chronic inflammation, with either complete or a very high grade obstruction of the cystic duct by calculi, as shown by the reports of Phemister, Rewbridge and Rudisill,[11] Phemister, Day and Hastings,[12] Cutler and Boggs[13] and others. It may occur as a separate deposit in the form of a stone, paste, or coarse sand, or as a layer on preexisting stones. That the condition is not uncommon is shown by the fact that it was observed 23 times in 510 consecutive cases of operatively removed gallbladders in the University of Chicago Clinics. The recognition of the condition was due, in part, to the fact that roentgenograms were made of most

of the excised gallbladders, and then special attention was given to materials casting a calcium shadow during the pathologic examination.

If bile has been completely excluded from the gallbladder for a long time, the calcium deposit will be white and the fluid scanty, clear and rich in mucus. If a small amount of bile enters, the contents will be somewhat pigmented, and the discolored calcium deposits may be easily overlooked. Inflammation of the gallbladder is either of low grade or absent during the period of calcium deposition. If the inflammation is more severe in the presence of cystic duct obstruction, hydrops or, rarely, empyema develops without calcium precipitation.

Appended are illustrative cases of pure calcium carbonate deposits in the presence of cystic duct obstruction by stone.

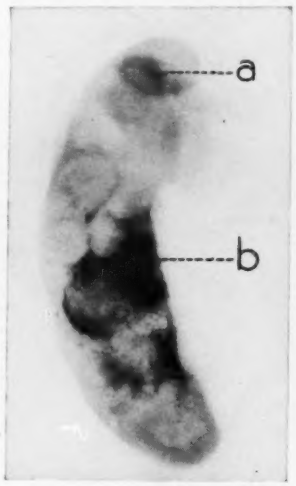


FIG. 1.—Case 1: Roentgenogram of gallbladder containing multiple cholesterol-pigment stones with one stone in cystic duct (a) showing calcium carbonate shadow (b) in lumen.

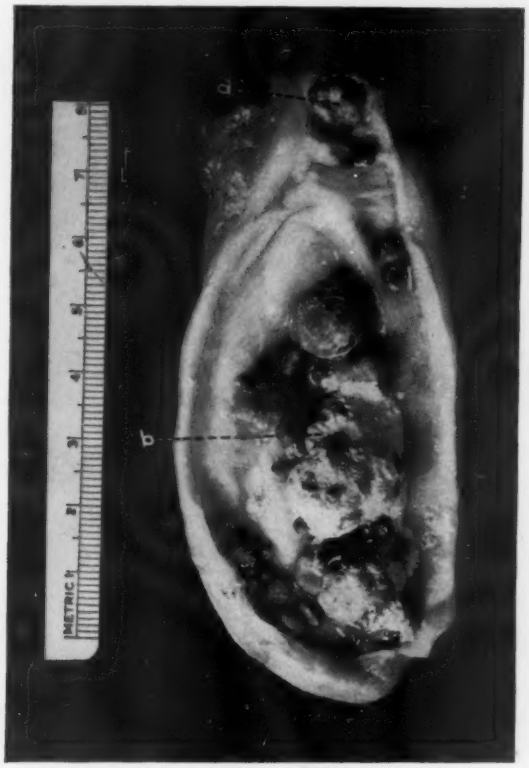


FIG. 2.—Case 1: Gallbladder shown in Figure 1, opened. (a) Stone in cystic duct. (b) Calcium carbonate deposit.

Case 1.—A. B., male, age 54, has had occasional attacks of epigastric pain during the past five years, with one of increased severity in the last few days. Cholecystography revealed a calcium shadow lying high in the gallbladder region and nonvisualization of the gallbladder by the dye. At operation, the gallbladder was thickened, distended with fluid, and showed evidence of mild acute inflammation. It contained stones and there was a stone in the cystic duct. Some clear fluid was aspirated and the gallbladder removed, including the stone-bearing portion of the duct. A roentgenogram of the excised gallbladder (Fig. 1) reveals the presence of faint shadows of multiple stones in the gallbladder and one stone in the cystic duct. In addition, there is a heavy shadow of material at the middle portion of the gallbladder and on the surface of some of the adjacent stones. On opening the gallbladder, a clear, viscid fluid escaped. It was found to contain numer-

ous brown, cholesterol-pigment stones, one of which was tightly wedged in the cystic duct. In addition, there was a white, soft deposit in the middle portion corresponding to the dense shadow shown in the roentgenogram. Some of it covered the surface of the adjacent stones (Fig. 2). Chemical examination revealed its inorganic content to consist of calcium carbonate. Roentgenographic powder diagrams revealed lines of calcium carbonate in the form of small crystals of aragonite and larger crystals of calcite. Cultures of the fluid and wall yielded nonhemolytic Streptococci. The gallbladder wall was moderately thickened and, microscopically, showed slight round cell infiltration. This was a

FIG. 3. FIG. 4.

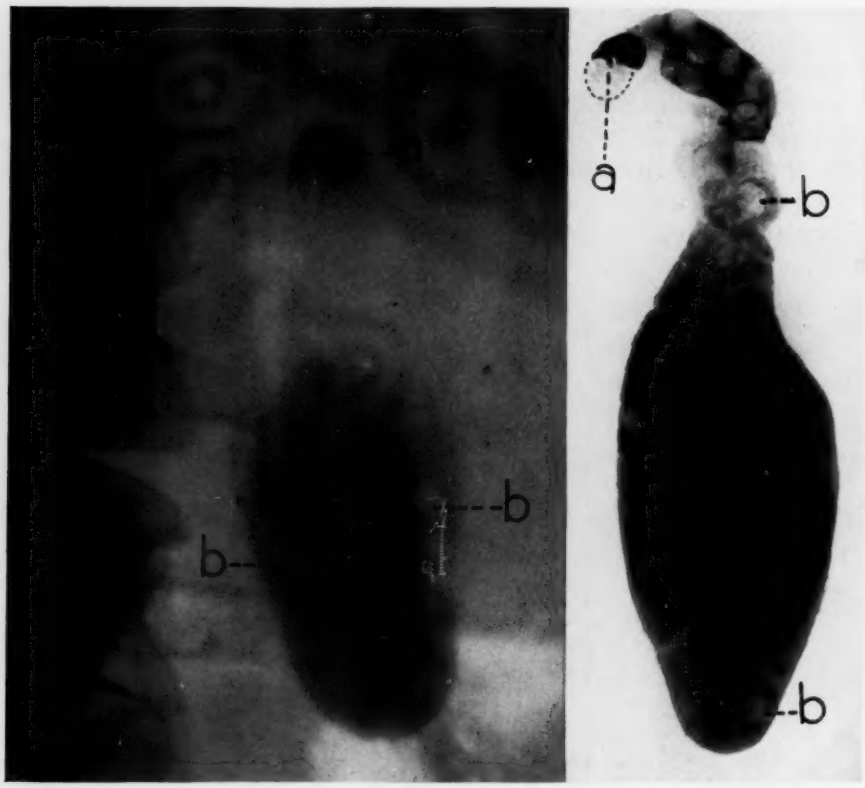


FIG. 3.—Case 2: Roentgenogram before dye administration. Radiopaque calcium carbonate on gallbladder side of stone in cystic duct (a), radiolucent shadow of cholesterol pigment stones (b) within calcium carbonate paste filling gallbladder.

FIG. 4.—Case 2: Roentgenogram of excised gallbladder. Cholesterol-pigment stone in cystic duct with half-moon-shaped calcium shadow on the gallbladder side (a), cholesterol-pigment stones (b) within calcium carbonate paste.

case of long-standing stones in the gallbladder, with calculous cystic duct obstruction and calcium carbonate deposition. There was superimposed a recent mild acute cholecystitis.

Case 2.—T. M., female, age 59, had attacks of epigastric distress, with belching and occasional nausea and vomiting for four years; no jaundice. Cholecystography revealed a dense radiopaque shadow before dye administration filling most of the gallbladder region, with several radiolucent areas within. There was a dense radiopaque shadow above, in the region of the cystic duct (Fig. 3). Roentgenogram following the administration of the dye showed no change in the shadows. At operation a stone was felt in the cystic duct. The gallbladder was about normal in size and there were adhesions constricting its proximal portion. The distal portion was filled with a soft mass. The adhesions were loosened and the gallbladder and stone-bearing portion of the duct re-

moved. A roentgenogram of the gallbladder (Fig. 4) revealed a radiopaque substance scattered throughout the fundus and the narrow proximal portion of the gallbladder. There were small circular radiolucent shadows in the gallbladder, most numerous in its narrow proximal portion. In the cystic duct there was the shadow of a stone, which was very radiopaque on the gallbladder side and radiolucent in its proximal two-thirds.

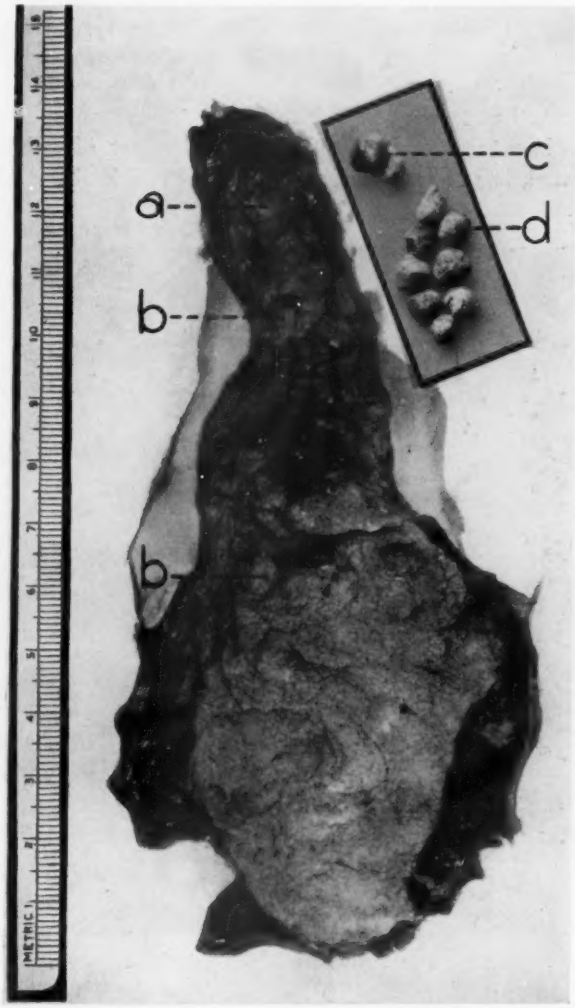


FIG. 5.—Case 2: Gallbladder and duct opened. Cystic duct stone (a), cholesterol-pigment stones embedded in calcium carbonate-mucus paste filling most of gallbladder (b). Inserted photograph of duct stone (c) and gallbladder stones (d).

The gallbladder and cystic duct were incised (Fig. 5). The gallbladder was filled with a slightly greenish, putty-like, viscid material. There were several brown stones, measuring 3 to 5 Mm. in diameter, scattered throughout it. The viscid material contained a grayish, thick, calcium deposit, and there was a thin white layer of calcium deposited on the surface of some of the stones. There was a cholesterol-pigment stone in the cystic duct, measuring roughly 1 cm. in diameter, and on its gallbladder side there was a heavy grayish deposit of calcium which cast the opaque shadow in the roentgenogram (Fig. 5,

a and b). The gallbladder, on microscopic examination, showed very slight cholecystitis. Cultures of the contents and wall remained sterile. Chemical examination of the putty-like mass revealed per 100 mg. of dry material, 34.5 mg. of calcium, 17.6 cc. of CO_2, and no phosphorus. This gives 86.25 per cent, if the calcium is calculated as calcium carbonate. Roentgenographic powder diagrams revealed lines of calcium carbonate in the forms of aragonite and calcite. The sequence of events was as follows: Cholesterol stones containing some pigment were laid down in the gallbladder. One of them had obstructed the cystic duct and a large pasty mass of calcium carbonate had then been precipitated in the gallbladder with only a very small amount of bile entering. There had been a heavy calcium deposit on the gallbladder side of the stone in the cystic duct and thin ring deposits of calcium on some of the other stones in the gallbladder.

Calcium carbonate precipitation in the gallbladder of animals, with the cystic duct ligated, has been reported by Wilkie[14] and by Phemister, Day and

FIG. 6. FIG. 7.

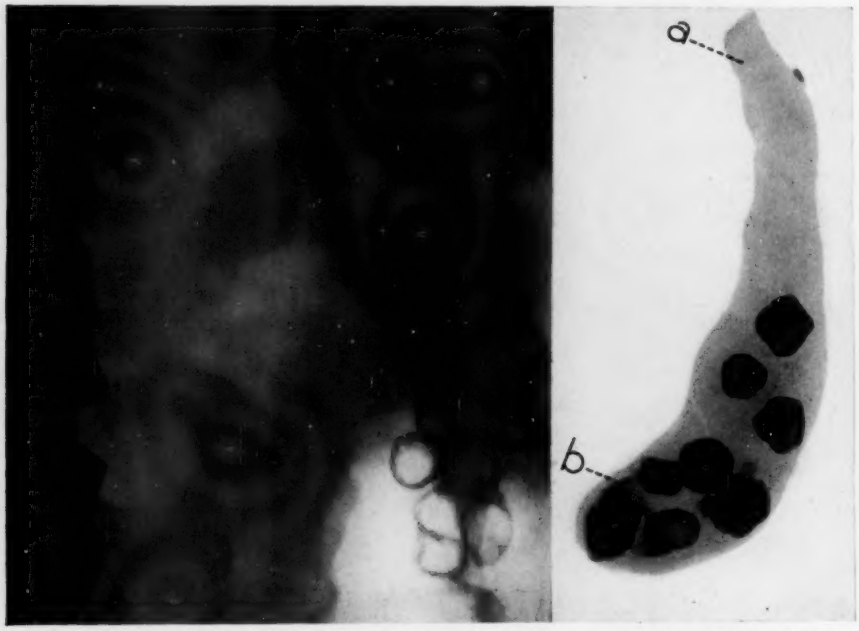


FIG. 6.—Case 3: Roentgenogram before dye administration showing eight ring shadows of calcium density. Gallbladder did not visualize with dye.

FIG. 7.—Case 3: Roentgenogram of excised gallbladder. Radiolucent stone in cystic duct (a), calcium deposit in lumen (b) separate from that on the eight stones.

Hastings. A review of the clinical and experimental evidence leads to the conclusion that the calcium carbonate comes from the wall of the gallbladder, since the bile was completely excluded from the gallbladder in some of the cases and in the animal experiments. R. Schoenheimer (unpublished) analyzed one pure calcium carbonate stone, at this clinic, for copper and found 0.005 per cent, whereas other gallbladder stones contained 0.3 to 1 per cent, indicating that the bile which is the source of copper was excluded from the gallbladder while the calcium carbonate was being precipitated.

Aschoff has reported the finding of pure pigment stones in the gallbladder, but their occurrence is extremely rare, and no mention has been made of their

relation to obstruction. Peel[15] analyzed such stones and found that they contained a high percentage of copper as compared with other gallstones.

Falling between the pure cholesterol stone on the one hand, which forms with mild stasis, and little or no inflammation, and the pure calcium carbonate stone on the other, which forms with complete or very marked obstruction and mild chronic inflammation, are the great group of mixed stones. They develop usually in aggregations in a pathologic gallbladder, the cause of which is disputed, but which authorities, as Naunyn[16] and Aschoff, have considered as infectious, although cultures are sterile in a large percentage of cases. There is a fairly definite relationship between their contents of bile pigments, calcium and cholesterol and the degree of associated obstruction of the outlet. There may be fluctuations with time in the amount of pathologic change in the gallbladder and in the amount of obstruction produced either by the stone or by the inflammation, as a result of which the composition of the different layers of the stones may vary accordingly. In general, it may be stated that as stasis increases in gallbladders the seat of calculi, whether single or multiple, any deposit which may then be precipitated on the calculi shows a tendency to increase in calcium content, and also in bile pigments up to a point where the obstruction becomes very marked and the source of the pigment, the bile, is too greatly reduced. Such secondary deposits are dark in color from the increased pigment and usually cast radiopaque ring shadows in roentgenograms. That they may be laid down during periods of high grade obstruction of the cystic duct by a stone which itself may not receive a deposit is illustrated in the appended case:

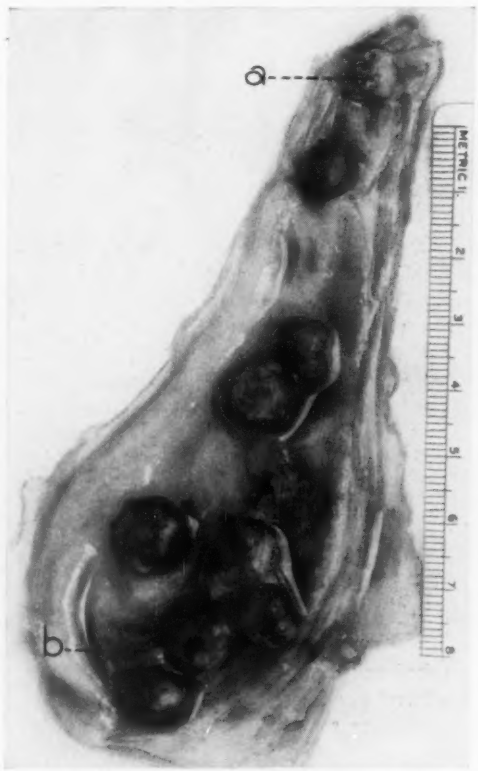


FIG. 8.—Case 3: Gallbladder opened. Soft cystic duct stone (a); separate calcium deposit in mucus (b). Gallbladder stones hard and dark green in color.

Case 3.—M. H., female, age 44, had mild attacks of gallstone colic for several years, the last being one week before admission. Cholecystography revealed eight ring-shaped radiopaque shadows in the roentgenogram before dye administration (Fig. 6), and non-visualization of the gallbladder by the dye. At operation, a stone was found in the cystic duct which could not be dislodged, and another one at the duct orifice which was easily moved back into the gallbladder. The gallbladder was removed along with the stone-

bearing portion of the cystic duct. It was little changed and slightly less distended than normally. A roentgenogram of the unopened specimen (Fig. 7) showed eight ring-shaped radiopaque shadows in the gallbladder and one radiolucent shadow in the duct. There were also small separate shadows of calcium density about three stones at the fundus of the gallbladder. On opening the gallbladder, it was found to contain a small amount of greenish-stained mucous fluid and eight dark green stones. The cystic duct contained a soft yellowish stone (Fig. 8). There was a small amount of grayish putty-like material about some of the stones at the fundus which cast the calcium shadow in the roentgenogram. Cultures of the bile and gallbladder wall remained sterile.

The stone in the cystic duct and one of the stones in the gallbladder were roentgeno-

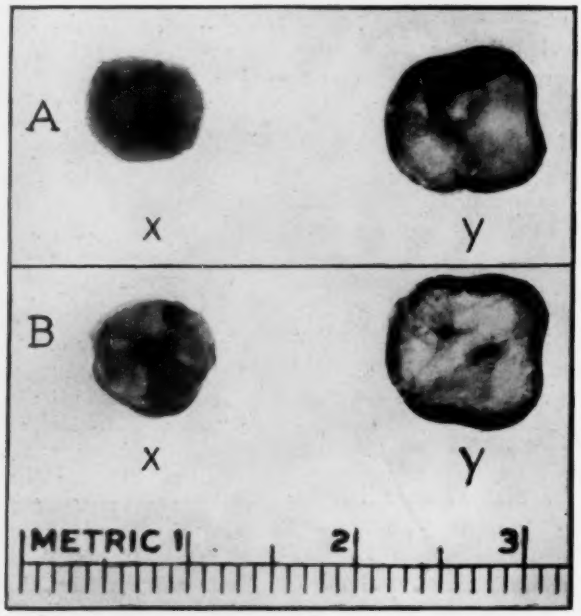


FIG. 9.—Case 3: A. Roentgenogram of the cystic duct stone (X), and one of the gallbladder stones (Y). B. Photograph of their cut surfaces showing a dark layer about the periphery of Y.

graphed and cut open, and their cut surfaces photographed (Fig. 9). The cystic duct stone and the interior of the gallbladder stone were alike composed of cholesterol, the former being somewhat discolored by pigment. The gallbladder stone was covered by a dark green, hard coat casting a radiopaque shadow.

TABLE I

ANALYSES OF THE CALCULI IN CASE 3

	Cystic Duct Stone	Gallbladder Stone, Center	Gallbladder Stone, Periphery
	%	%	%
Ether extraction (weight)	81.2	86.2	38.7
Pure cholesterol (colorimeter)	35.7	40.3	15.4
Calcium	0.19	0.47	5.45
Phosphorus	—	—	0.05
Pigment	Trace	Trace	+ Amount not determined

Chemical analyses (Table I) showed the coating on the gallbladder stone to consist of cholesterol, calcium and a small amount of pigment while its interior and the cystic duct stone were composed essentially of cholesterol. If the calcium is reckoned as present in the form of $CaCO_3$ it amounted to 13.6 per cent. Roentgenographic powder diagrams of the stone from the cystic duct and of the central portion of a stone from the gallbladder showed lines of cholesterol and none of inorganic substances, while the shell of the latter showed lines of calcium carbonate in the forms of aragonite in a large amount and calcite in a small amount.

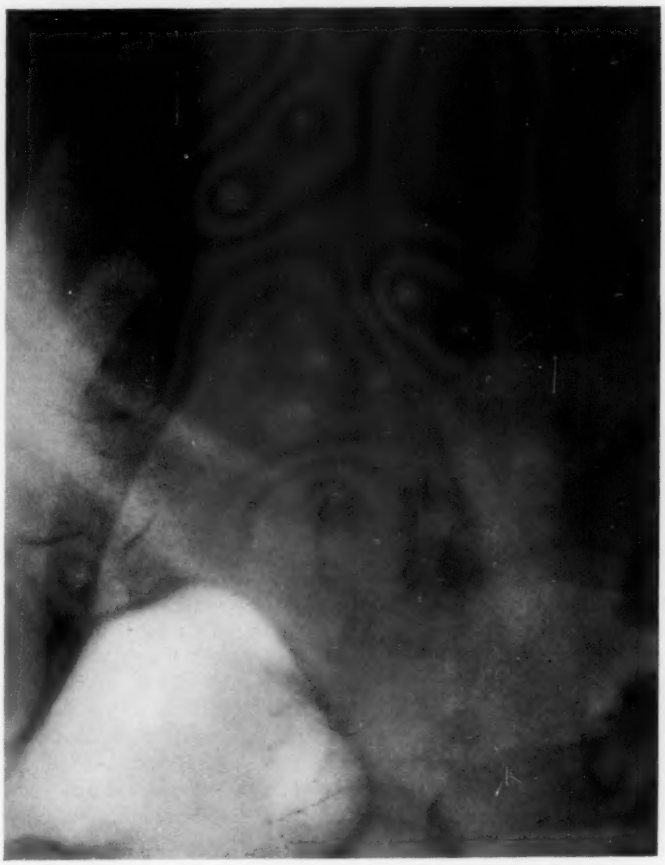


FIG. 10.—Case 4: Ring- and cylinder-shaped radiopaque shadows in gallbladder region. Gallbladder failed to visualize with dye.

The pathogenesis of the process was as follows: An aggregation of nine cholesterol stones formed in the gallbladder. One of them entered the cystic duct, producing marked obstruction; a layer consisting essentially of calcium carbonate, bile pigment and cholesterol was then deposited on the eight stones in the gallbladder, but the stone in the duct being more freely bathed in unobstructed bile did not receive a similar coating. At some stage in the process the obstruction had been very marked, and pure calcium carbonate in the form of a paste had been deposited in the fundus of the gallbladder.

Further proof of the importance of obstruction in the causation of secon-

dary deposits rich in calcium and pigment on preexisting stones is the fact that if a gallbladder is largely filled and more or less partitioned by a row of stones, and if the outlet becomes incompletely blocked, calcium and pigment may be deposited on the stones in increasing amounts proceeding from the outlet to the fundus apparently as a result of increasing stagnation in the compartments created by the stones. No mention of this occurrence has been encountered in the literature, but it has been observed in varying degrees in five instances since it first came to notice one year ago, and is illustrated by the appended two cases:

Case 4.—N. S., female, age 51, had attacks of epigastric and right upper quadrant pain, radiating to the back, at irregular intervals for several years, and entered the hospital four days after the onset of a mild acute attack. Cholecystography revealed in the roentgenogram taken previous to dye administration, ring and cylindrical shaped radiopaque shadows in the region of the gallbladder, and there was nonvisualization by the dye (Fig. 10). At operation, a thick-walled, subacutely inflamed gallbladder, largely filled with stones, was found, and there was a stone in the beginning of the cystic duct. The gallbladder was removed and was found to contain, in addition to the calculi, a small amount of yellow mucinous fluid, cultures of which remained sterile; cultures of the wall showed diphtheroid bacilli. The stone in the first portion of the cystic duct was nodular and yellowish-gray in color. The three stones in the gallbladder were faceted and showed increasing pigmentation from ampulla to fundus (Fig. 11). The stones were roentgenographed (Fig. 12), sectioned with a fine jeweler's saw, and drawn in colors, to show the external and cut section appearances (Fig. 13). The center of each composite stone in the gallbladder consisted of a cholesterol-pigment stone, similar to the one in the cystic duct. The four stones had formed in the gallbladder and one had entered the duct, after which the three in the gallbladder had grown from deposits which increased from cystic duct to fundus in pigment content, as shown by gross appearance and in calcium content, as shown by the roentgenogram. The roentgenogram revealed no calcium shadow on the stone in the cystic duct, an opaque cup-shaped calcium shadow on the distal half of the second stone, ring and band-shaped shadows on the third stone, and double ring-shaped shadows on the fourth stone, with a small radiopaque shadow at its center. A thin slice was cut from each stone. The slices were roentgenographed and samples taken from the different regions for chemical analyses, as indicated somewhat roughly in Figure 14. In general, they show the composition of the four central stones and of the secondary deposits, some samples consisting largely of the zones casting radiolucent shadows and others largely of pigmented material, casting radiopaque shadows. It was difficult to separate the materials sharply into radiopaque and radiolucent samples; the radiograms and roentgenographic powder diagrams afford, therefore, a better indication of the distribution of the calcium carbonate than do the chemical analyses. The four original central stones are rich in cholesterol and low in pigment and calcium with the exception of the nucleus of the fourth stone, in which there had apparently been a secondary deposit of calcium. This had probably taken place in a cavity created by swelling and shrinkage, as is not uncommonly found in gallstones. While the results of the analyses are somewhat inconstant, the secondary peripheral deposits laid down during duct obstruction showed proportionately much more pigment and calcium, and less cholesterol than the central portions.

Roentgenographic powder diagrams were made at the periphery of the stone in the fundus of the gallbladder. They showed lines of a finely divided material having a structure resembling that of dahlite and apatite, which are complex compounds of tricalcium phosphate and calcium carbonate.

Case 5.—D. M., female, age 51, gave a history of occasional mild attacks of gallstone colic over a period of ten years, and was admitted to the hospital two days after

FIG. 11.

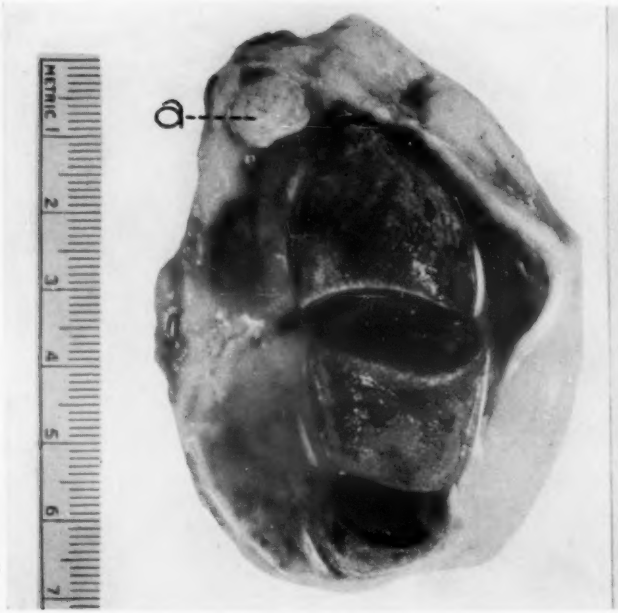
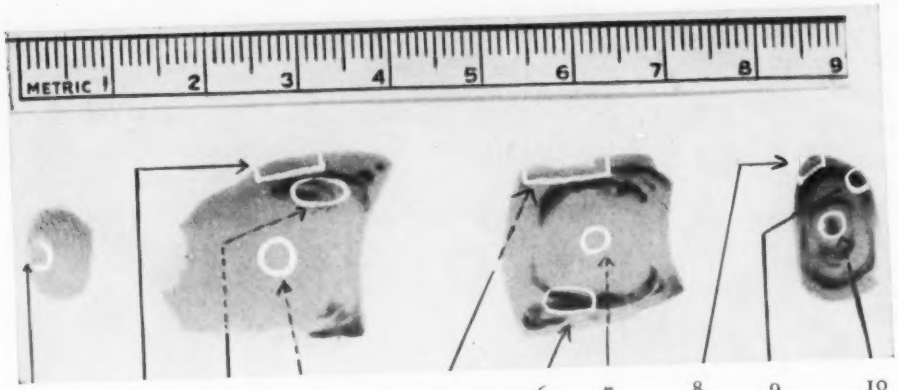


FIG. 12.

FIG. 13.

FIG. 11.—Case 4: Gallbladder opened. (a) Stone in cystic duct.
FIG. 12.—Case 4: Roentgenogram of stones. Cystic duct stone (a) casts no calcium shadow. Calcium shadows cast by distal end of second stone and by third and fourth stones.
FIG. 13.—Case 4: External and cut surface appearance of stones. Cystic duct stone (a) of same appearance as central portion of the three composite stones in the gallbladder. External layers of latter show increased pigmentation away from cystic duct.



	1	2	3	4	5	6	7	8	9	10
	%	%	%	%	%	%	%	%	%	%
Ether extraction (weight)	51.2	32.8	54.3	64.1	28.8	41.1	53.8	41.0	44.4	59.1
Pure cholesterol (colorimeter)	39.3	26.1	41.3	49.7	21.6	31.1	41.0	34.9	33.9	33.0
Calcium	0.3	0.9	1.9	0.5	0.8	3.6	0.4	0.5	4.0	1.4
Phosphorus	0.2	0.2	0.1	0.2	Trace	0.7	0.2	0.3	0.6	Trace
Pigment	Trace	27.7	12.8	2.5	3.4	20.0	10.4	36.0	40.0	Trace

FIG. 14.—Case 4: Roentgenogram of slices of stones, arranged from cystic duct (a) to fundus (b) showing, roughly, regions analyzed chemically, and an appended tabulation of the analyses.

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the onset of an attack. Cholecystography revealed a row of radiopaque shadows in the roentgenogram before dye administration, the one in the fundus region being the most dense. There was no visualization of the gallbladder by the dye (Fig. 15). Six weeks later, after subsidence of the acute cholecystitis, the gallbladder was removed. It was long, thick-walled, and filled with four large stones. A roentgenogram (Fig. 16) shows radiopaque calcium shadows in the second, third and fourth stones, increasing in intensity away from the radiolucent stone at the ampulla. On opening the gallbladder, one stone was found engaged in the ampulla. There were about 10 cc. of serosanguineous fluid that contained numerous black particles about 1 Mm. in diameter. Cultures yielded a microaerophilic Streptococcus. The stone in the ampulla was yellowish-red in color. The other three stones were faceted and externally were increasingly dark in color from am-

FIG. 15.—Case 5: Gallstones in gallbladder casting radiopaque shadows of increasing density toward fundus (a). Nonvisualization of gallbladder by the dye.

pulla to fundus. They were sectioned longitudinally with a jeweler's saw, and color drawings to scale were made to show the distribution of the pigment (Fig. 17). The centers of all four stones consist of a yellowish (cholesterol) zone, measuring 1½ to 2 cm. in diameter. Apparently, the four original stones had formed simultaneously, and the proximal stone then obstructed the ampulla, after which there were lamellated secondary deposits on all of them. The deposit on the proximal stone appears grossly to be of essentially the same material as the original; that on the second stone showed slightly more brownish pigmentation; and that on the third stone showed yellowish-brown pigmentation of the proximal, and deep brown to black pigmentation of its distal portion. That on the fourth stone showed brown to black pigmentation. Slices were cut from the four stones, roentgenographed, and samples taken roughly of the various portions for chemical analyses (Fig. 18). The central stones were rich in cholesterol and low in calcium and pigment. The periphery of the stones showed calcium increasing in amount from the ampulla to

Fig. 16.

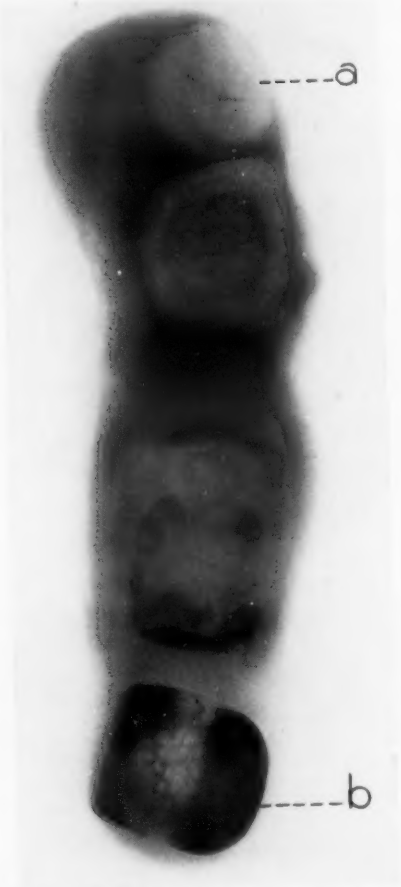
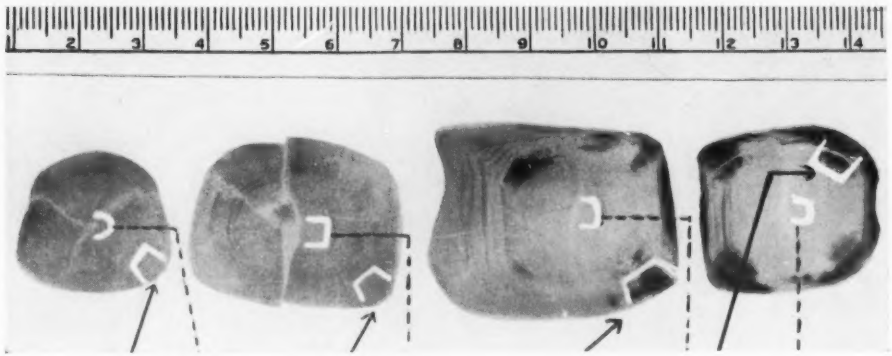


Fig. 17.

Fig. 16.—Case 5: Roentgenogram of exised gallbladder shows calcium shadows in increasing depths in stones from the ampulla (a) to fundus (b).
Fig. 17.—Case 5: Exterior and cut sections of stones; centers of all four stones similar. Surface deposits show increased pigmentation from ampulla (a) to fundus (b).

a



b

	1 %	2 %	3 %	4 %	5 %	6 %	7 %	8 %
Ether extraction (weight)	83.6	76.1	75.0	84.3	70.5	82.3	59.7	69.3
Pure cholesterol (colorimeter)	55.5	64.5	51.4	55.2	43.2	41.7	30 5	46.4
Calcium	1.0	Trace	Trace	0.3	1.1	0.5	6.9	0.3
Phosphorus	Trace	Negative	Trace	Trace	1.0	Negative	3.2	Negative
Pigment	Trace	Trace	0.3	0.1	1.2	0.1	2.2	Trace

FIG. 18.—Case 5: Roentgenogram of slices of stones, arranged from ampulla (a) to fundus (b) showing regions analyzed chemically, and an appended tabulation of the analyses.

fundus. While the pigment of the periphery of the stones also increased in amount from the ampulla to the fundus, the figures show a much smaller amount than would be expected from the gross appearance (Table III). This suggests that some of the pigments were not detected by the method of analysis employed or other coloring matter was present.

Roentgenographic powder diagrams were made of the periphery of the stone in the fundus of the gallbladder. They revealed lines identical with those found in the stones in Case 2.

When one end of a gallstone is engaged in the ampulla of the gallbladder, it is not uncommon for calcium and pigment to be deposited on the other

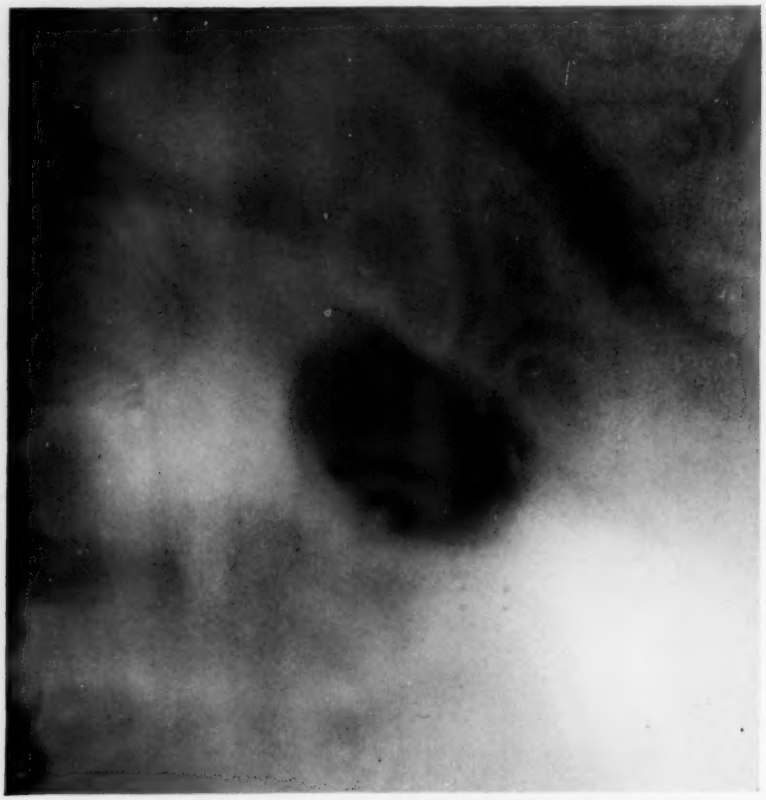


FIG. 19.—Case 6: Gallstone shadow; gallbladder did not visualize with dye.

end as a result of the stagnation which it produces. This has been seen in four cases and is illustrated by stone 1 in Figure 24.

Surface deposits rich in calcium and pigment are often found on both single and multiple stones without any accompanying stone obstruction of the cystic duct or ampulla being found at operation or autopsy. The question arises whether they were laid down during a period of inflammatory obstruction or temporary stone obstruction. That obstruction may be a factor, is supported by the finding that in the great majority of cases of cholelithiasis with stones casting a radiopaque (calcium) shadow there is nonvisualization of the gallbladder by the dye, as reported by Graham[10] and Phemister, Day and Hastings.[12] The condition is illustrated by the following case:

Case 6.—M. P., female, age 66, had had indefinite attacks of epigastric distress at intervals for four months. A roentgenogram (Fig. 19) revealed a large radiopaque shadow in the gallbladder region, with an oval center which was less dense than the thick periphery. There was no change in the shadow after dye administration. At operation, no stone was found in the cystic duct. The gallbladder was removed. It was moderately thickened and contained a small amount of dark, stringy bile and a dark

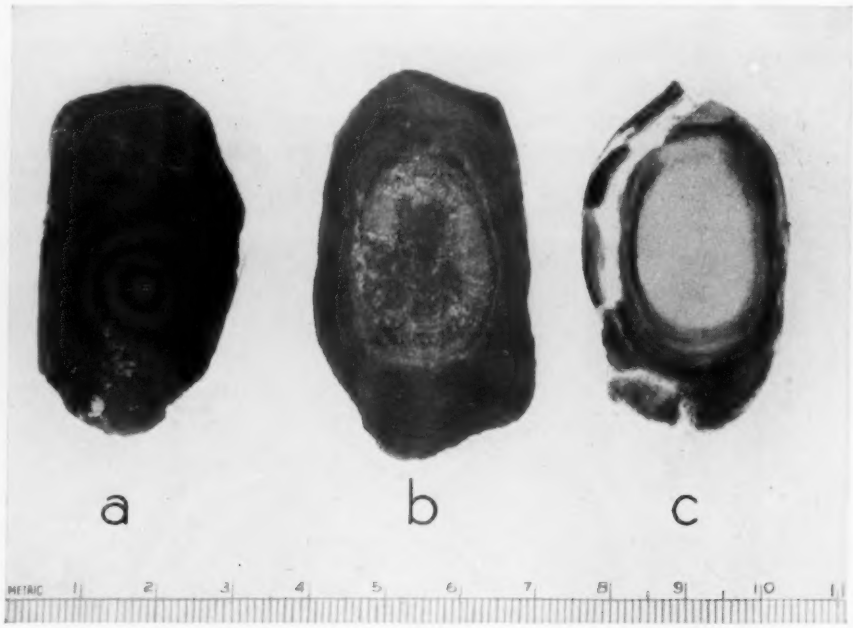


FIG. 20.—Case 6: (a) Photograph of exterior and (b) of cut surface of stone. (c) Roentgenogram of slice. Central portion is a cholesterol stone. Dark periphery consists of pigment, calcium carbonate, and cholesterol.

TABLE IV

ANALYSIS OF THE CALCULUS IN CASE 6

	Periphery	Center
	%	%
Ether extraction (weight).....	18.5	55.5
Pure cholesterol (colorimeter)...	8.7	44.2
Calcium.....	4.96	0.25
Phosphorus.....	2.0	0
Pigment.....	5.8	Trace

brown oval stone, measuring 5.2x3 cm. (Fig. 20a). Section of the stone showed it to consist of a grayish, crystalline, cholesterol center and a thick greenish-brown, lamellated periphery (Fig. 20b). A roentgenogram of a somewhat fragmented slice (Fig. 20c) reveals a radiolucent center and a lamellated radiopaque periphery, showing that the calcium density is confined to the pigmented portion.

Chemical analysis (Table IV) showed the central portion rich in cholesterol. The peripheral portion revealed proportionately less cholesterol, but substantial amounts of calcium, pigment and phosphorus. Roentgenographic powder diagrams of the peripheral portion showed lines of calcium carbonate, chiefly as calcite but also as aragonite and vaterite B.

Little attention has been given to the condition of the cystic duct in such cases, but it is possible that a careful examination at operation or autopsy would reveal evidence of some degree of inflammatory obstruction. The possibility of functional obstruction or dyskinesis of both the cystic duct and the ampulla of Vater has been advocated by Westphal,[17] and of kinking adhesions and anomalous folds of the cystic duct by Cole.[18] Secondary changes in gallbladder, including infection, complicating one of these conditions might lead to calculus formation with the deposition of layers rich in pigment and calcium.

While single or multiple mixed stones may remain uniform in composition, fluctuations in cholesterol, pigment and calcium content may occur from their incipiency, giving rise to many layers which vary both in chemical

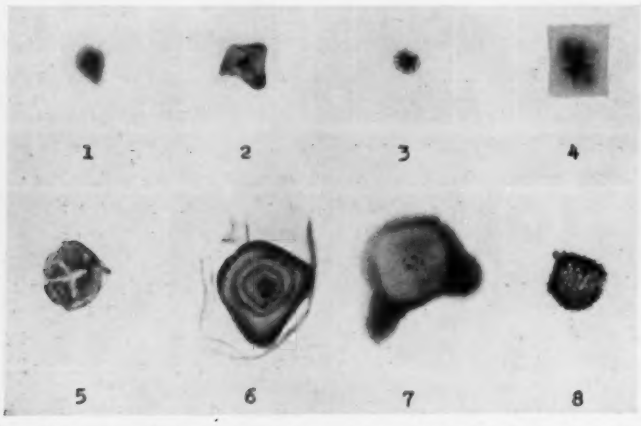


FIG. 21.—Roentgenogram of stones removed from different gallbladders showing different arrangements of radiopaque calcium carbonate shadows.

composition and in thickness; thus a nucleus may be rich in calcium and pigment, or there may be one or more layers, rich in calcium and pigment, deposited at intervals as the stone grows, which alternate with layers made up of cholesterol and pigment only. Rarely, there is a radiating arrangement of the materials rich in calcium and pigment. Figure 21 shows roentgenograms of stones removed from the gallbladders of different patients, in whom no stone obstruction of the cystic duct was found. Their dense areas indicate that they contained calcium, variously distributed in nucleus, internal and external layers, and even in rays and in clefts. There is little concrete evidence at hand as to the presence or absence of obstruction at the time the calcium was deposited. In the cases analyzed, the calcium was present along with pigment and cholesterol in somewhat the same proportions as found in the layers of stones in the preceding cases in which there was stone obstruction of the duct. The similarity suggests that these deposits were laid down during periods of temporary obstruction by inflammation or, less likely,

by spasm or by stones which subsequently passed the cystic duct. The star-shaped deposits of calcium in clefts of multiple stones (Fig. 21, 4) that have formed, according to Bauer,[19] as a result of swelling followed by shrinkage and transformation from spherical to polyhedral forms, may be further evidence of the rôle of stagnation in calcium deposition, since the fluid permeating the clefts becomes stagnant. That very high grade inflammatory obstruction of the cystic duct may occur is demonstrated by the occasional finding of a mucocele of the gallbladder in which bile has been completely excluded by duct swelling for a long period of time as in the following case:

Case 7.—W. E., male, age 36, had had vague distress in the epigastrium and right upper quadrant, coming on usually at night, lasting for two or three hours. There was residual soreness for 12 to 24 hours, and the attacks gradually increased in frequency over a period of eight months. Cholecystography revealed no radiopaque shadow in the

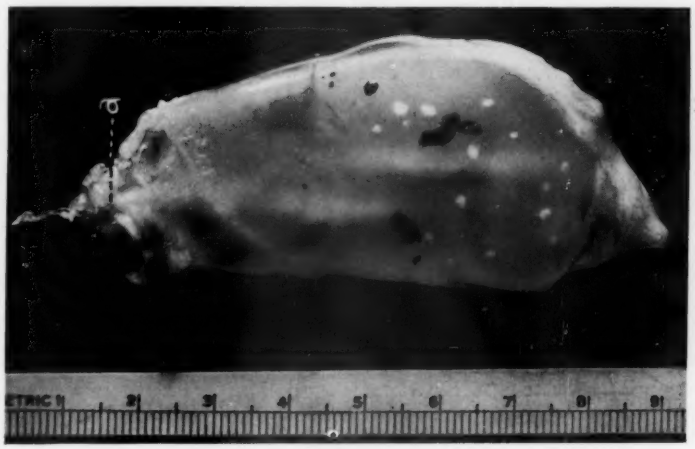


FIG. 22.—Case 7: Mucocele of the gallbladder resulting from inflammatory obstruction of cystic duct (a).

gallbladder region, and there was nonvisualization of the gallbladder by the dye. At operation, a moderately thickened gallbladder, somewhat smaller and much more tense than normal, was found. There were no stones palpable, either in the gallbladder, or cystic or common duct. The gallbladder was removed. On section, it was filled with clear, very thick mucus which was irregularly dotted with white and a few black, soft, flocculent areas. No stones were found (Fig. 22). Smears of the black areas showed them to consist very largely of pigment and a few cholesterol crystals. On the other hand, the light specks consisted very largely of cholesterol, with a small amount of pigment. The short portion of the cystic duct, which was excised, was swollen, but when cut open a lumen was present. Cultures of the gallbladder and mucus were sterile. Microscopic sections of the gallbladder showed slight edema and round cell infiltration of the wall.

Obstruction in this case was of such high grade that calcium carbonate might well have been thrown out as a free deposit in the gallbladder, since the mucus which it contained was freer from biliary content than was found in some of the observed cases of pure calcium carbonate deposition in the gallbladder.

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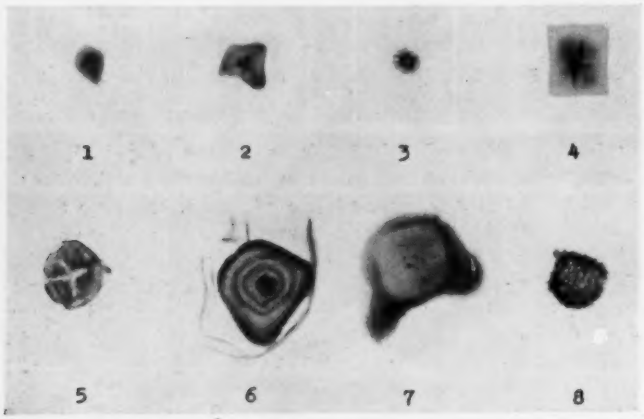

FIG. 21.—Roentgenogram of stones removed from different gallbladders showing different arrangements of radiopaque calcium carbonate shadows.

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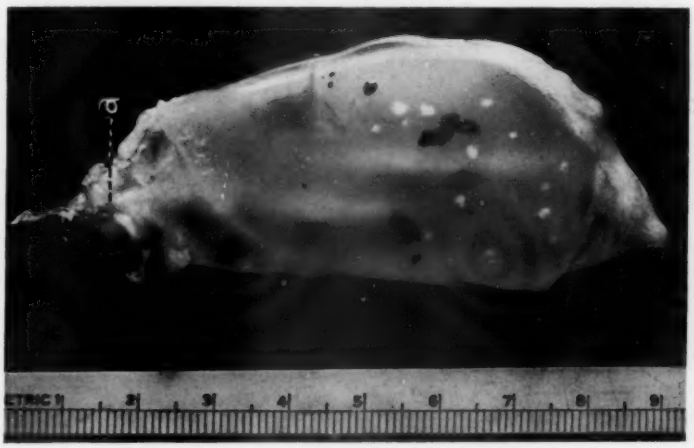

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Stone Formation in the Bile Ducts.—In contrast to the marked variation in composition of stones formed in the gallbladder are the relative uniformity of composition of stones formed in the bile ducts and the paucity, or absence, of calcium carbonate.

Stone formation there is usually preceded by stone formation in the gallbladder, and it is set up after calculi have passed into the common duct with resultant cholangic obstruction and infection. Rarely, it may occur independent of cholecystolithiasis, as in cirrhosis of the liver (McIndoe and Judd[20]), or in carcinomatous obstruction of the ducts (Lampert and McFetridge[21] and Marshall[22]), and the stones may even form in the intrahepatic radicals. When the stones have been laid down in the presence of calculi which came from the gallbladder, the question arises as to whether or not it is possible to distinguish between the two. However, stones formed in the ducts after removal of the gallbladder and of stones from the common duct, afford opportunity to obtain accurate information about the composition of the material laid down there. The following three cases of this type have been studied:

Case 8.—B. R., female, age 59, married, had had an attack of gallstone colic with jaundice, in 1932. She was operated upon by Dr. A. F. Henning, who removed the gallbladder, which contained several light to brown stones, and three brown stones were removed from the common duct. The patient remained well for two years, after which she had occasional attacks of pain in the epigastrium, nausea and vomiting lasting for short periods and sometimes followed by jaundice. For three months before admission to the University of Chicago Clinics, December 13, 1936, she had had attacks of pain accompanied by chills and fever and followed by jaundice. The examination on admission showed her in fairly good general condition, afebrile, and free from jaundice and bile in the urine. There was moderate tenderness in the right hypochondrium. At operation, December 16, 1936, stones were felt in the common duct, which was inflamed and markedly enlarged. On opening the choledochus, a large stone was found just above the ampulla of Vater. It was removed along with about 150 smaller stones which were in the dilated common and hepatic ducts above. A catheter was then inserted and many small stones, of similar appearance, were washed from the intrahepatic radicals. Cultures of the bile showed *B. coli*, Streptococci and *B. proteus*. T-tube drainage was established and maintained for three and one-half weeks. The ducts were irrigated daily and several small stones were subsequently washed from them. The patient has since remained free from symptoms. Figure 23 is a photograph of the stones removed from the ducts. Attempts to pass a probe through the ampulla of Vater were unsuccessful.

Section of the large stone and of several small stones showed them to consist of a uniformly dark, greenish-brown, soft material. There was no separate center in the large stone to suggest that it represented a gallbladder stone that had been left in the common duct at the previous operation.

Chemical analysis revealed cholesterol (impurities included) 65.8 per cent by weight, and 55.9 per cent by colorimetric determination, bile pigments 12.7 per cent, calcium, a trace (not measurable), phosphorus negative. Roentgenographic powder diagrams revealed no lines of calcium carbonate or other inorganic substance.

Since all the stones were of uniform structure and composition, and since the stones washed from the intrahepatic ducts must have been formed there, it is safe to say that these were calculi which were formed within the ducts.

Failure to pass a probe into the duodenum may have been due to temporary swelling but it may have indicated some degree of permanent narrowing of the ampulla which, as well as the infection, was a factor in causing the stone formation.

Case 9.—C. R., male, age 53, was first admitted May 3, 1930, with the following history: In 1912, he had had recurrent attacks of right upper quadrant pain and a cholecystostomy was performed, at which time a large cholesterol stone was removed which the patient saved (Fig. 24, 1). There were recurrent attacks after three years which, in 1918, were associated with jaundice. A cholecystectomy was then performed, and the pathologist's report was that the gallbladder contained several stones. About three years later he began to have mild attacks of right upper quadrant pain which recurred irregularly until 1928, when they became more severe and were accompanied by chills, fever and jaundice. He entered the hospital in 1930 because of recent attacks.

Physical examination was essentially negative aside from tenderness in the right

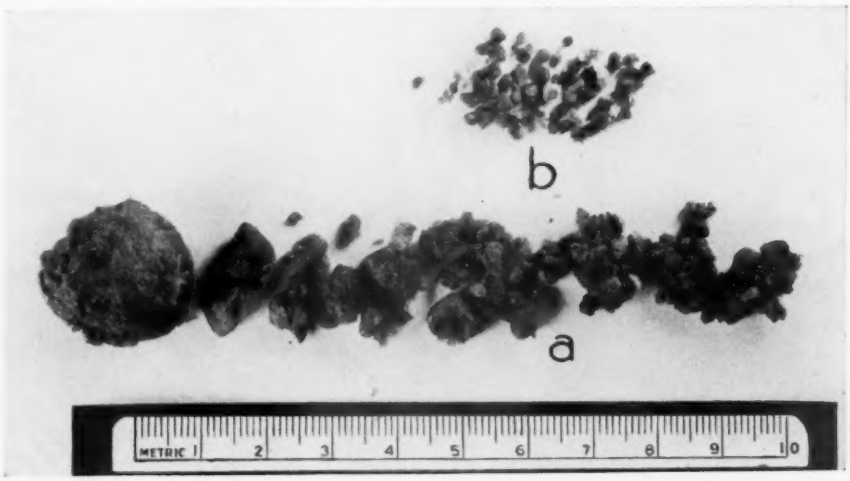

FIG. 23.—Case 8: Stones removed from common and hepatic ducts (a) and intrahepatic ducts (b); which formed after cholecystectomy and choledocholithotomy.

upper quadrant. Cholecystography revealed no shadow of either gallbladder or calcified stone. At operation a dark stone, about 2 cm. in diameter, was removed from the common duct (Fig. 24, 3). He remained well for over a year and then had attacks of right upper quadrant pain. In March, 1935, an attack was followed by jaundice which continued in mild form until readmission three months later. Physical examination was then essentially negative except for slight jaundice. A roentgenogram of the biliary region was negative for radiopaque stone shadows. At operation, June 21, 1935, seven large reddish-brown stones were removed from the dilated and infected common and hepatic ducts (Fig. 24, 4). The ampulla of Vater was patent. Cultures yielded *B. coli*, Streptococci and *Cl. welchii*. There was T-tube drainage for one month. Beginning three and one-half months after operation, the patient had an attack of right upper quadrant pain and slight jaundice. Similar attacks recurred and he was again operated upon, February 28, 1936, at which time a soft reddish-brown stone, 1½ cm. in diameter, was removed (Fig. 24, 5). A catheter was introduced into the hepatic radicals and numerous very small dark stones resembling sand were washed out. The ampulla of Vater was patent. Cultures of the fluid yielded *B. coli*, hemolytic Diplococci and *Cl. welchii*. T-tube drainage was maintained for five months subsequently with daily irrigations. Small dark pigmented stones were occasionally washed from the duct over a

period of weeks. The patient has remained well for two years following the removal of the T-tube.

A roentgenogram was made of the stones removed at the first, third, fourth and fifth operations (Fig. 24). The only shadow of calcium density is that on the surface of

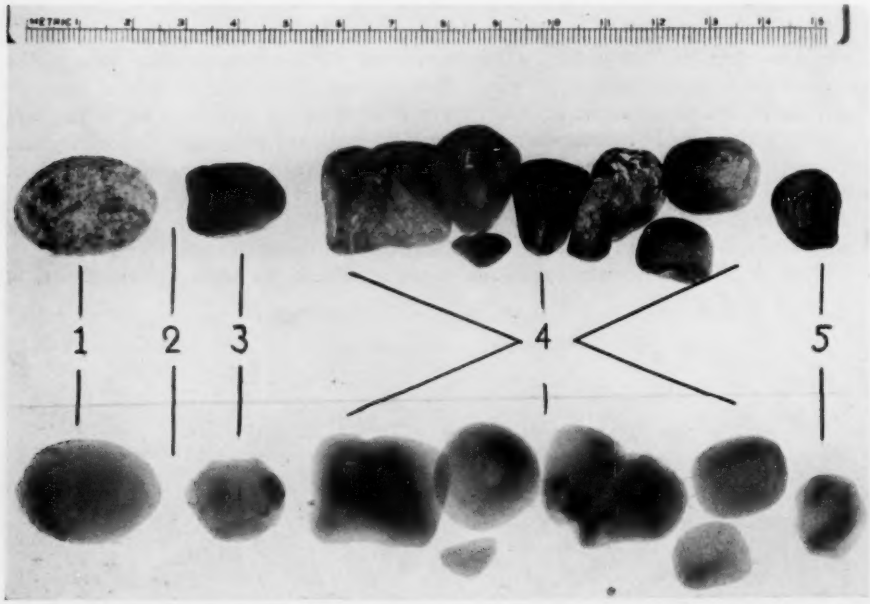

FIG. 24.—Case 9: Photograph above and roentgenogram below. Stone removed from gallbladder (1). Cholecystectomy in interval (2). Stone removed from common duct at third operation (3); fourth operation (4); and fifth operation (5).

TABLE V

ANALYSES OF THE CALCULI REMOVED AT THE VARIOUS OPERATIONS UPON CASE 9

Stone	First Oper. No. 1912	Third Oper. No. 3152 Periphery	Third Oper. No. 3152 Center	Fourth Oper. No. 8934	Fifth Oper. No. 9771 Mixture	Bile Duct Washings
Ether extraction (weight).....	76.0%	60.5%	78.7%	55.0%	34.5%	36.0%
Pure cholesterol (colorimeter)..	49.7%	31.7%	42.4%	49.5%	19.9%	Not Determined
Calcium.....	Rt. end neg. Lft. end 3.0%	Negative	Negative	1.05%	1.1%	1.8%
Phosphorus.....	Negative	Negative	Negative	Negative	Negative	Negative
Pigment.....	0.3%	9.1%	2.1%	21.2%	14.8%	42.0%

one end of the stone removed from the gallbladder which probably had been deposited while the other end was obstructing the ampulla. Sections were made with a jeweler's saw of the stones removed at the first and third operations and of one stone from the fourth operation (Fig. 25). The one removed at the first operation is a solitary choles-

terol stone with a thin, hard crust on one end. The stone from the common duct at the third operation consists of a thick, reddish-brown outer layer deposited on a light yellow central stone. That from the common duct at the fourth operation is reddish-brown except for a dark black débris at the center, which possibly represents an old blood clot. Since the outer layer of the second stone resembles the third stone and also the one removed at the fifth operation, it is highly probable that it was deposited in the duct on the lighter central stone which had migrated there from the gallbladder. This view is supported by the fact that the patient had been jaundiced before the second operation at which the gallbladder containing multiple stones was removed. The very small pigmented stones washed from the intrahepatic ducts at the last operation were the same in color and consistency as the larger stones. The chemical analysis of the stones is given in Table V.

Roentgenographic powder diagrams showed lines of calcium carbonate in the form of vaterite and calcite in the surface coating on the left end of stone 1, and none in the stones that were formed in the common and hepatic bile ducts. They showed cholesterol lines in all the stones.

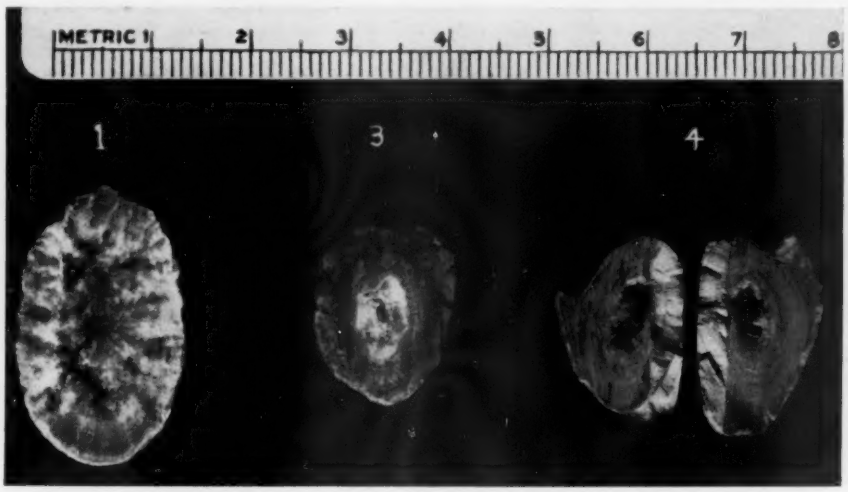

FIG. 25.—Case 9: Sections of stones from first, third and fourth operations.

In brief, the stones known to be formed in the common, hepatic and intrahepatic ducts were rich in cholesterol and bile pigments and very low in calcium. The center of the first stone removed from the common duct appeared to have come from the gallbladder and to have been the obstructing factor which helped to set up stone formation in the ducts. Prolonged drainage and irrigation of the ducts after the last operation appeared to help clear up the infection and get rid of the stone forming tendency.

Case 10.—R. F., male, age 66, entered the hospital in October, 1932, with a history of attacks of gallstone colic extending over a period of three years, most of which had been accompanied by fever and jaundice. He was then in a free interval but the urine contained a trace of bile. At operation, October 14, 1932, a thickened and adherent gallbladder, free from stones, was removed. The dilated and thickened common duct was opened and eight stones removed from it (Fig. 26, a). There appeared to be pocketing of the duct near the ampulla of Vater and one stone was removed from it with great difficulty. A probe was passed into the duodenum. The common duct drainage was con-

tinued for 21 days. About one year later the patient had recurrence of the right upper quadrant pain accompanied by slight chills, fever and jaundice. These continued at irregular intervals for about two and one-fourth years, at which time the trouble grew worse and the jaundice became persistent. He was readmitted to the hospital, April 23, 1935, with mild jaundice and bile in the urine. At operation, May 6, 1935, one large and about ten soft, small, dark reddish-brown stones were removed from the common duct (Fig. 26, b). The large stone was engaged in a pocket just above the ampulla of Vater and was extracted with difficulty. Cultures of the bile yielded a heavy growth of *B. coli*, Staphylococci and Streptococci. The duct was closed with catheter drainage; leakage of bile and duodenal contents, however, developed subsequently, resulting in death from peritonitis, eight days after operation. Autopsy revealed suppurative peritonitis, a large pocket of the first portion of the common duct and a few soft brown stones in ducts within the liver.

Sections were made of the stones removed at the first operation. They consisted of a white crystalline interior coated by a dark reddish-brown layer, measuring 1 to 2

FIG. 26.—Case 10: Stones removed from common duct at first operation (a), and at second operation (b).

Mm. in thickness. Section of the large oval stone, 3 cm. long, removed at the second operation, revealed a central white portion similar to the centers of the stones removed at the first operation. This was covered by a reddish-brown intermediary layer of the same thickness and nature as the coating of the stones at the second operation and by a thick brown layer outside this, which evidently represented a deposit on a stone left in the pocket at the first operation. The other stones from the second operation were composed of this same brown material. Figure 27 shows a cross section of one of the small stones removed at the first operation and of the large stone removed at the second operation after much of its soft surface portion had crumbled off.

Chemical analyses were made of the light central and reddish-brown peripheral portions of the stones, shown in Figure 27, removed at the two operations, and of the soft brown stones removed from the intrahepatic ducts at autopsy (Table VI).

Roentgenographic powder diagrams were made of the portions of stones that were analyzed chemically. They showed lines of cholesterol but no lines indicative of calcium carbonate or other inorganic contents.

The order of development in this case appears to have been as follows: An aggregation of cholesterol stones formed in the gallbladder, which migrated to, and obstructed, the common duct. Then stone formation was set up in the ducts and a reddish-brown coat of pigment and cholesterol was deposited

on each stone. Cholangeitis was present. Following operation, at which one stone was left in the common duct, there was continued infection and stagnation in the duct pocket. This led to further stone formation in the intra- and extrahepatic ducts of the same general character as the deposit previously laid down on the stones from the gallbladder.

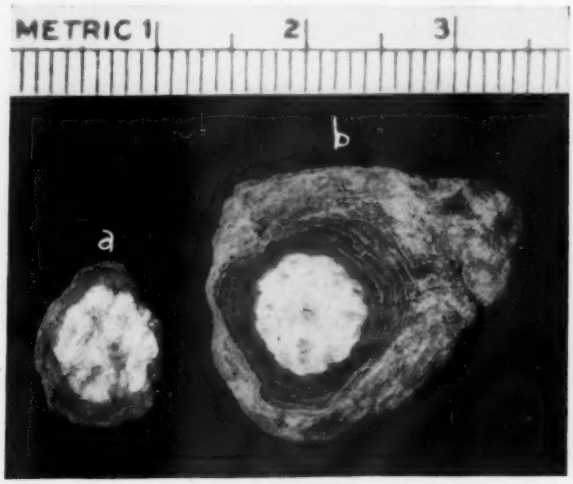

FIG. 27.—Case 10: Sections of stone from first operation (a) showing cholesterol center and periphery of cholesterol pigment, and from second operation (b) showing center stone of same nature as (a) with deposit on outside.

TABLE VI

ANALYSES OF THE CALCULI REMOVED AT THE TWO OPERATIONS UPON CASE 10

Stone	(a) Center %	(a) Periphery %	(b) Center %	(b) Intermediary %	(b) Periphery %
Ether extraction (weight).....	91.5	31.8	90.0	34.8	56.8
Pure cholesterol (colorimeter).	46.9	16.8	54.1	19.7	21.8
Calcium.....	0.52	0.95	0.64	0.49	1.08
Phosphorus....	—	—	—	—	—
Pigment.....	Trace	25.5	Trace	25.3	22.1

Discussion.—In all three cases, obstruction of the common duct by a stone or stones migrating there from the gallbladder appears to have preceded the setting up of stone formation in the ducts. Infection was present in all cases and obstruction and infection appeared to have been causative factors in the reformation of stones after gallbladder and common duct stones had been removed. However, additional causative factors that were active in the gallbladder were possibly also active in the ducts. There was little variation in the composition of the stones, which consisted in the three cases of pigment and cholesterol with very little or no calcium.

Reformation of stones after cholecystectomy and choledocolithotomy, should

be more frequent if the stone forming tendency has already been set up in the ducts, and if some degree of infection and obstruction persist postoperatively. Benign stricture of the common or hepatic ducts, resulting from injuries at operation, are usually not accompanied by stone formation within the ducts. In nine cases operated upon in this clinic, there was the presence of a small amount of brownish mud in two cases, which resembled, grossly, small amounts of material present in the three cases of recurrent stones in the ducts. The failure of development of stones in such cases may be related to the fact that injury is usually of a duct not containing stones and consequently neither infected nor obstructed nor possessing the stone forming tendency.

SUMMARY.—Stones found in the gallbladder vary greatly in their contents of cholesterol, pigment and inorganic calcium salts, one important cause of which is variation in the amount of associated obstruction of the cystic duct. Stones very rich in cholesterol may form in the gallbladder when stasis is mild, as judged by the great frequency of dye visualization, and when inflammation is mild or absent, as judged by pathologic examination. With increasing chronic obstruction of the cystic duct there is a tendency for increasing amounts of calcium and bile pigments to be laid down on the preexisting stones in the gallbladder.

If large stones partition the gallbladder, causing increasing stagnation within, from ampulla to fundus, there is a tendency for any further growth of the stones to consist of materials which increase in pigment and calcium contents from ampulla to fundus. With complete, or almost complete, obstruction of the cystic duct in the presence of low grade chronic cholecystitis, calcium carbonate alone may be precipitated from the gallbladder fluid as a whitish deposit either about the preexisting stones or as a separate mass.

In contrast with these findings, stones formed in the bile ducts vary relatively little in building materials consisting of bile pigments and cholesterol with very little or no calcium. Obstruction is an important cause of stone formation in the ducts, since it is usually set up in the presence of a stone from the gallbladder which has lodged there. Persistent cholangeitis, with some degree of inflammatory obstruction, appear to be factors in the reformation of stones in the ducts after cholecystectomy and choledocholithotomy.

Calcium is present very largely as calcium carbonate, which may be in the specific crystalline forms of aragonite, calcite or vaterite B, as shown by roentgenographic powder diagrams. However, calcium was present in two cases of gallbladder stones, partitioning and obstructing the gallbladder in a form resembling dahlite.

The source of the calcium carbonate is the wall of the gallbladder, in case it is thrown down within the gallbladder while the cystic duct is completely obstructed by a stone.

Its source is also the wall of the gallbladder, when it is deposited in

layers on gallbladder stones in the presence of high grade but incomplete stone obstruction of the cystic duct as in Case 3. The findings that calcium is laid down in the gallbladder, when its outlet is obstructed, and that stones formed in the ducts contain little or no calcium, are highly indicative that the calcium salts of gallstones are derived from the wall of the gallbladder, and that little or none come from the bile.

The source of the cholesterol of calculi formed in the common duct after removal of the gallbladder is doubtless the bile.

The view that the cholesterol of gallstones formed in the gallbladder is also derived from the bile is favored by the finding of a decreased cholesterol content of gallstones formed with increased obstruction of the common duct, while their calcium and pigment contents are increased; also by the absence of cholesterol deposition when calcium carbonate is deposited within the gallbladder in the presence of complete obstruction of the cystic duct.

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FURTHER EVIDENCE THAT PANCREATIC JUICE REFLUX MAY BE ETIOLOGIC FACTOR IN GALLBLADDER DISEASE*

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IT IS obvious to anyone who has had much experience with biliary tract surgery that there are factors concerning biliary tract pathology which are not understood at the present time. As recently as January, 1938, Clute,[2] in an editorial in the Journal of Surgery, Gynecology and Obstetrics, stated: "Most students of the pathology of acute cholecystitis now agree that obstruction to the cystic duct is the primary lesion in this disease, and that *infection, when it occurs in these cases, is a secondary phenomenon* which is dependent on this obstruction for its development." Also: "Such patients reveal at operation tensely distended, edematous, red gallbladders. Yet their course following immediate cholecystectomy is generally very much like the course of any laparotomy for a non-inflammatory lesion." It has also been observed that when cultures are made of such gallbladders, they frequently are sterile. No doubt in many cases stones may be found impacted in the neck of the gallbladder or in the cystic duct, but not uncommonly no stones will be found and one at once must speculate upon the cause of the peculiar type of reaction. Judd likened it to a chemical process. Such an experience about ten years ago led me to suspect a pancreatic juice reflux as a possible etiologic factor, and, in 1931, the results of experimental work were published.[12] In 1937, further observations and conclusions were given in a communication.[13] The details of the experiments and conclusions previously presented will be omitted in this communication; however, a few of the pertinent points will be mentioned to clarify the subject.

It was proved experimentally that pancreatic juice when introduced in the gallbladder of the dog invariably produced pathologic changes in the wall of the gallbladder. These varied from degenerative changes characterized by extensive necrosis to complete gangrene and regenerative changes, displaying inflammatory reaction with interstitial, lymphoid and papillary hyperplasia. It was also shown that India ink which had been introduced into the terminal end of the common duct of the dog was later recovered in the gallbladder. Evidence was presented to show that known and unknown factors are present which may activate the pancreatic juice, and that the degree and nature of the alteration in the wall of the gallbladder may depend upon a degree of activation and dilution of the pancreatic juice, stasis most likely being an essential factor. Attention was also called to the frequency of an anatomically proven common pathway between the pancreatic and biliary tracts.

It is the purpose of this communication to further elaborate upon phases

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of the theory that pancreatic juice reflux may be an etiologic factor in gallbladder disease.

It has been proved by anatomic study that in a fairly large percentage of cases a common pathway between the pancreatic and biliary passages is present, allowing a reflux of the pancreatic juice into the biliary ducts. A compilation of statistics from eight authors reporting upon examinations of 652 speci-

TABLE I

Author	Total Number	Number with Common Pathway	Per Cent
Opie	100	11	11
Baldwin	90	20	22
Schirmer	48	22	47
Belou	50	27	54
Ruge	43	32	75
Letulle and Nattan-Larrier	21	8	38
Cameron and Noble	100	74	74
Mann and Giodano	200	90	45
	652	284	43.4

mens shows a common pathway in 284 instances, or 43.4 per cent (Table I). The question may be raised as to whether in the living a common pathway is physiologically present. Cholangiography, or radiologic visualization of the biliary tree after the introduction of an opaque material, has been developed to a marked degree during the past few years. In studying these cholangiograms, it is noted that in quite a number of instances the pancreatic duct is visualized and in the presence of obstruction at the papilla, the pancreatic duct may be dilated (Figs. 1 and 2). Our series is too small to report at the present time; however, we have noted visualization of the pancreatic duct, and in studying cholangiograms which have appeared in current articles and in private collections, its presence has been detected. Doubilet and Colp[4, 5] have recently reported that in a series of 22 cases in which common duct drainage was instituted, eight cases showed significant to large amounts of amylase in the duct drainage; in fact, one case for a brief period of time drained almost pure pancreatic juice from the common duct. They also report that in all cases with common duct drainage in which the pancreatic duct could be visualized radiologically considerable quantities of amylase were found in the drainage from the ducts. There seems to be sufficient material available to warrant the conclusion that frequently a physiologic common pathway is present between the pancreatic and biliary ducts and that there is present in such instances a reflux of pancreatic juice into the biliary tract.

It may be postulated without fear of criticism that if a stone is impacted at the ampulla, and if the stone does not obstruct the orifice of the pancreatic duct in the presence of a common pathway, pancreatic juice may mix with the biliary contents of the common duct, and finally reach the gallbladder. It is a fact that stone impaction at the ampulla is uncommon in the average case of

cholecystitis; however, surgeons are reporting increasing numbers of instances of stones in the common duct when operating for cholecystitis, Lahey recently placing the figure at 21 per cent. Free stones in the common duct afford an excellent opportunity for temporary occlusion at the sphincter, or their presence may cause a low grade papillitis with a spasm of the sphincter. However, to prove the thesis, one must look further for a cause for obstruction, one which precedes the formation of stones.

FIG. 1 FIG. 2

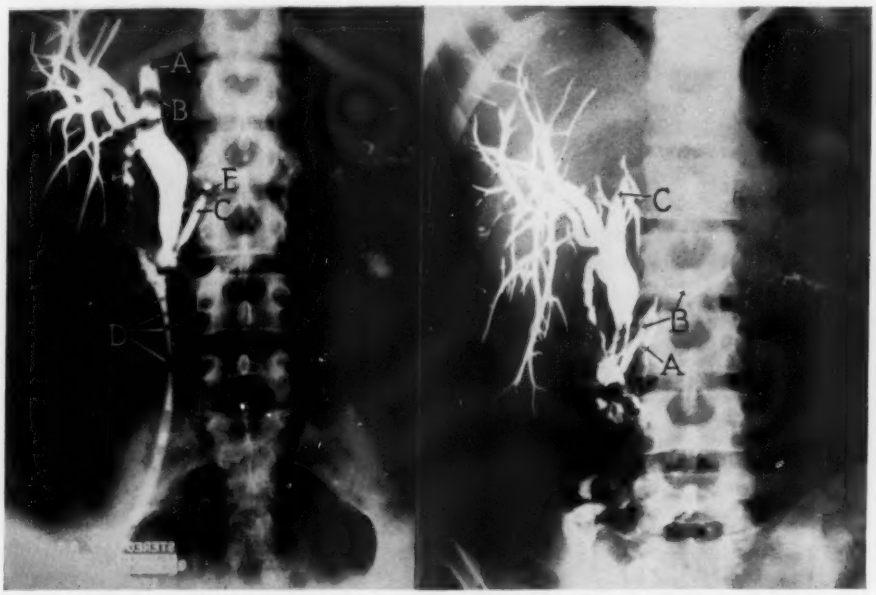

FIG. 1.—Cholangiogram made after the removal of common duct stones. Anteroposterior position. (A) Abrupt ending of the left hepatic duct as if obstructed. (B) Vacuoles which resemble those produced by stones. (C) Pancreatic duct. (D) Air globules in the catheter. (E) Constriction in the pancreatic duct which may be due to spasm.

FIG. 2.—Cholangiogram of same patient as in Fig. 1 taken in the posteroanterior position about five minutes later. (A) Accessory pancreatic duct. (B) Pancreatic duct showing the median portion more distended than the terminal due either to spasm of the duct or organic stenosis. (C) Left hepatic duct well visualized. (It will be noted that the vacuoles shown in Fig. 1 are no longer present, demonstrating sources of error in the technic of cholangiography and in the interpretation of cholangiograms. The vacuoles in Fig. 1 were caused either by localized accumulations of duct contents which did not fuse with the oil suspension, or by air. The presence of air in the catheter in Fig. 1 is evidence that air was being introduced. The abrupt ending of the left hepatic duct in Fig. 1 may be due to position since a change in position was followed by an immediate filling.)

It is conceded by all physiologic investigators that a true sphincter is present at the terminal end of the common duct, also that there is a normal or physiologic mechanism which controls the evacuation of the bile as it is secreted by the liver. It is further presumed that a sphincter or some sphincteric action is necessary for the gallbladder to fill and allow it to concentrate its contents, and eventually to expel it into the common duct and subsequently into the duodenum. The normal mechanism is believed to be that when the gallbladder contracts, the sphincter relaxes. There may be variations in this mechanism. It is common knowledge that following cholecystectomy, the sphincter becomes incompetent, the intraductal pressure falls, and there is

more or less continuous flow of bile into the duodenum during digestion. This would indicate that there is a close physiologic relationship between the gallbladder and the sphincter. The sphincter is responsive to various drugs. Hunt, Hicken, and Best[8] and Doubilet have shown that morphine causes marked and continuous spasm of the sphincter. Doubilet and Colp have shown that the instillation of dilute hydrochloric acid into the duodenum brought about a prompt rise in the intraductal pressure, and that the instillation of a magnesium sulphate solution caused a fall in the pressure. They have also proved that the spasm produced by the instillation of dilute hydrochloric acid into the duodenum can be abolished by atropine. These experiments indicate that the sphincter is susceptible to various influences. Ivy[9] states that any condition which increases the tone of the duodenum retards the flow of bile into the duodenum, and that which decreases the tone of the duodenum and promotes normal peristalsis favors the flow of bile into the duodenum. There is sufficient evidence to prove that there are variations in the sphincter mechanism which are at variance with the normal and lead to biliary stasis. Ivy has reported one such case—a patient with previously normal cholecystogram and normal roentgenologic findings in the alimentary tract suffered from acute right upper abdominal and epigastric distress, and mild icterus with an enlarged tender gallbladder. The patient reported feeling a tumor in the region of the gallbladder. Five to ten minutes after the hypodermic injection of 1/60 gr. of atropine, the distress and tumor disappeared, and several hours later, a stool consisting of almost pure dilute bile was evacuated. It is evident that this disturbance or dissociation in the biliary motor mechanism, termed biliary dyskinesia or dyssynergia, is sufficient to produce symptoms, and may supply the mechanism for pancreatic juice reflux in the presence of a common pathway.

It has been shown by us that India ink which was introduced into the terminal end of the common duct of the dog was later recovered in the gallbladder. The question may arise as to the mechanism involved. Ivy has stated that the gallbladder "is a reservoir of small volume but of large capacity." Under normal conditions, it may concentrate its contents 10 to 1. In the presence of an obstruction at the papilla, be it organic or functional, the pressure within the common duct increases. Since the pancreatic juice is under higher secretory pressure than the bile, the level of pancreatic juice in the common duct will ascend toward the liver. During this time the contents of the gallbladder are being concentrated, allowing more common duct contents to enter. It is but a matter of time until pancreatic juice enters the gallbladder.

The agent which activates the pancreatic juice is still not definitely determined. Since the gallbladder is an offshoot from the intestinal tract, embryologically, it is believed by some that its mucosa secretes enterokinase. If this is true, the amount is exceedingly small. It is known, however, that substances other than enterokinase may activate pancreatic enzymes. This problem was discussed in some detail in a previous communication. It has been proved that

normal bile will not activate pancreatic juice (Doubilet); also it has been shown that a substance liberated by broken down cells may act as an activating agent (Lombardi). Lombardi,[11] Dragstedt[7] and others[12, 13] have shown that sterile pancreatic juice is inactive, but that when it is contaminated, it becomes active, Lombardi believing that the activating substance is derived from the micro-organism. He has termed this substance bacteriokinase. Ivy[10] noted a violent reaction of the mucosa of the gallbladder after the introduction of 15 cc. of 1/10 normal sodium bicarbonate solution into the gallbladder. Since pancreatic juice has approximately the same degree of alkalinity as 1/10 normal sodium bicarbonate solution, it may be reasoned that the alkaline pancreatic juice when it comes in contact with the gallbladder in sufficient quantity and concentration may produce a chemical irritation of the mucosa with destruction of cells. A specific substance liberated by the disintegrated cells then activates the pancreatic enzymes. Other factors may be present as proposed by Lombardi.

The relative infrequency of involvement of the walls of the common duct was explained by Brackertz[1] to be due to an inordinate amount of elastic tissue beneath the mucosa. This theory cannot be accepted since elastic tissue beneath the mucosa would not protect the mucosa against the digestive action of activated pancreatic juice. The explanation is most likely on the basis of an increased resistance of the mucosa to an alkaline medium, since the liver bile is alkaline, constant dilution of the pancreatic juice by liver bile and the lack of stasis or prolonged and continuous contact.

Observations during the past few years lead to the conclusion that many cases of cholecystitis as well as common duct and gallbladder stones can be accounted for on the basis of a pancreatic juice reflux. It is suggested that consideration be given to endocholedochal section of the sphincter of Oddi described by Colp, Doubilet and Gerber[3] as a possible form of treatment in some cases.

With the pancreatic juice reflux theory of the causation of gallbladder disease in mind, it is recommended that some widespread observations be carried out:

(1) Repeated examinations for amylase should be made of the drainage in all cases of gallbladder and common duct drainage.
(2) In all cases of gallbladder and common duct drainage, cholangiographic studies should be made in an endeavor to visualize the pancreatic duct.
(3) In all cases of gallbladder and duct disease, note should be taken of the possibility of an early history suggestive of biliary dyskinesia.

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A STUDY OF THE RESULTS OF SURGICAL TREATMENT OF PEPTIC ULCER

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A FOLLOW-UP CLINIC was organized in the Surgical Department of the Presbyterian Hospital in 1916. For the past 22 years, the Senior members of the staff, with their associates, have spent one full morning each week in this clinic, studying and recording the results of surgical therapy. As a result of the clinic, the intimate relationship between doctor and patient has deepened with time.

An idea of the effort made by the surgeons and clinic aides, and of the resulting response made by the patients in a large metropolitan community, is gained from the following figures: namely, in the year 1935, 5,983 patients were asked to return to the general Surgical Follow-Up Clinic; of these, 5,034 did return, 883 responded by letter, and only 66, or about 1 per cent, were lost. It is only by such high incidence of interviews between doctor and patient, months or years after operation, that accuracy in the estimation of the results of therapy can be approximated.

The follow-up visits in many types of cases are discontinued after a reasonable length of time. In the special clinic for the study of peptic ulcer, however, as in certain other types of cases, no case is discontinued; hence follow-up studies are possible over long periods of time. Of equal importance, we believe, is the fact that each case is followed in continuity, that is, the continuous postoperative course is charted rather than just the clinical, symptomatic picture at stated intervals. For convenience these records are maintained graphically.

A standard method for recording follow-up results must, of course, be agreed upon in any such study. The method in use in our clinic gives the result from anatomic, symptomatic and economic standpoints. In the present study of peptic ulcer the symptomatic results, only, are under consideration. There are four main groups into which all results are divided: Groups 4 and 3, which form the satisfactory ones, and Groups 2 and 1, the unsatisfactory. Group 4 includes only the cases with no symptoms whatever at any time since operation. Group 3 includes only cases with no significant symptoms, or in other words a very satisfactory group, in which only the mild digestive disturbances to which normal man is heir may occur.

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Groups 2 and 1 include all unsatisfactory cases, Group 1 representing the least satisfactory results of all, including the failures. In addition, for purposes of this critical review, in a given case, if an unsatisfactory record is noted at any time during the postoperative course, then this case is *permanently* dropped from the satisfactory groups, as will be seen later.

The purpose of this study was to review individually, and as a group, the cases which had passed through our hands, in order to obtain, if possible, a foundation upon which to base the treatment of new cases in the future. We had found that none of us was consistent in his recommendations for therapy, largely because, as a group, we did not know accurately the results of our recommendations in the past. In the 20-year period which this study covers, some of our patients had improved after operation. In others, the benefit was doubtful or clearly absent. By a careful appraisal of the follow-up records we hoped to be able to separate, with reasonable accuracy, the individuals that had been treated successfully from those that had not. If, then, we could find a set of factors peculiar to the successful or unsuccessful groups, we might obtain standards to guide us in selecting cases for operation and in choosing which type of operation to employ for individual cases.

Statistics derived from the study of groups are notably unreliable as a basis for the treatment of any individual, and it is always an individual for whom one must make recommendations. In this study, however, we have had the advantage of knowing well almost every patient within the group, so that we have been able to consider the records on the charts in the light of what we knew from contact with the patients themselves, in a way that an independent reviewer could not do. If the record seemed misleading, we could verify or correct it. In this way, some of the dangers inherent in dividing patients into artificial groups could be minimized.

The cases included in this study are all those who were operated upon at the Presbyterian Hospital for gastric or duodenal ulcer, between the years 1916 and 1935 inclusive, excepting the few that were operated upon elsewhere, previously. They, therefore, include the patients of some 25 surgeons. No one technic was followed. After operation, all patients, with the few exceptions noted in the tables, were seen at follow-up visits in the clinic or privately, at which times they were questioned as to their symptoms since their previous visits, examined, and frequently roentgenographed. They were then rated at each visit anatomically, symptomatically, and economically on the basis used in our Follow-Up Clinic and explained above. As noted before, it is the symptomatic rating with which this study is concerned.

In 1935 and 1936, the records from the charts were transferred to cards, samples of which are herewith reproduced. The cards have advantages in filing and reviewing that the charts cannot have. They furnish graphically, and at a glance, the important details of histories which may be of many years' duration. Anyone who has struggled through a voluminous record, attempt-

ing to get a conception of the case as a whole, will appreciate the value of these cards as adjuncts to the charts. From the cards and the charts and our knowledge of the patients themselves, we have compiled the accompanying tables.

We have used certain terms in the tables that need definition. We have included under gastric ulcer only those ulcers that did not directly involve the duodenum. Most of these were of the familiar lesser curvature kind. All other ulcers we have called duodenal, whether they were clearly in the duodenum, or in the pylorus, or spread out into both. The criteria have been explained for rating the cases as symptomatic Group 4, 3, 2 or 1. Groups 4 and 3 represent the satisfactory results; Groups 2 and 1 the unsatisfactory. Where the information was not obtainable as to rating, we have used the term "Insufficient Follow-Up." This does not mean, of course, that we consider the follow-up on all other cases "sufficient," but merely that we have enough information about them to rate them with confidence, as of the date of this report. In postoperative deaths, we have included all cases that died in the hospital following operation, whether the death was thought to be due directly or indirectly to the operative procedure. Only one other patient, who died at home three months after leaving the hospital, could in reason be added to this list.

Finally, in some tables we have divided the cases into those showing before operation: (1) Obstruction, (2) Bleeding, or (3) Pain, as the outstanding symptom. Under Obstruction are those cases which had 50 per cent or more six-hour retention, or any 24-hour retention determined roentgenologically, with the added provision that this degree of retention had to be persistent and unrelieved at the time of operation. Under Bleeding we have placed those cases in which there was convincing evidence of gross hemorrhage at any time before operation. We did not include in this group the cases that had only occasional evidence of occult blood. Cases which had both obstruction and bleeding we have placed under Obstruction with the notation that they also bled. All cases having neither obstruction nor bleeding we placed under the heading Pain, as this was their outstanding symptom.

The separation of cases into these three groups—Obstruction, Bleeding, and Pain—can never be wholly accurate. Hemorrhages in some individuals may easily go unobserved. The degree of obstruction may vary, so that an individual meeting the standards of the Obstruction group at one period might fail to meet them at another. Conceding all this, it is nevertheless true, as the tables show, that the groups so chosen responded differently to forms of therapy, notably to gastro-enterostomy, so that it is now possible to select with greater assurance the individuals upon whom to perform this operation, and equally important to discontinue its use in cases comparable to those in which it has proven unsatisfactory. The justification for the

grouping, therefore, lies in the aid it should give in the management of future cases.

In appraising the operative result in each case, we have raised two questions: First, has the individual *at any time* since his operation had significant symptoms of ulcer; and second, in how many *years* since his operation has he had such symptoms? The answers to the first we have noted under "Results According to Cases," and to the second under "Results According to Years." According to the first standard, if an individual in a single instance had symptoms which caused him to be rated as unsatisfactory, he was then, forever, classed as unsatisfactory, because it is clear that the operation did not rid him of his disease. But the same individual may have been wholly free of symptoms for many years before and after his single fall from grace. It is unfair not to distinguish him from the patient, who, year after year, showed no benefit from operation. The tables showing the "Results According to Years" take account of this difference. The case of B. F., Charts No. 5 and 6, a facsimile of whose record is given below illustrates this point. For eight years, B. F. came to the Follow-Up Clinic, the picture of health, denying any symptoms of gastro-intestinal distress, although before operation, for four years, he was rarely free of pain. He then appeared almost in collapse as the result of a severe hemorrhage which might well have been fatal. How much benefit from operation had he? Much, according to years; as a "cure," none. While he is an extreme example, he demonstrates the difficulty of estimating fairly the results of therapy in this variable disease, and the need for adopting more than one standard of judgment. In general, even reading the two sets of tables together, a conception of the results of surgery is obtained which may be unduly pessimistic. Many of the patients that we have labelled "unsatisfactory," when asked whether they have received benefit from the operation, reply with conviction, "Yes." Lacking acquaintance with them over the years before operation, as intimately as we have known them after, it is impossible for us to know whether to agree with them.

The analysis of the ulcer cases in the manner described above has done much to fulfill its purpose. Faced with a new patient, we may now state, with fair assurance, into what group he falls, *i.e.*, Obstruction, Bleeding or Pain. In addition, we believe that we can advise more intelligently the operative procedure indicated in his case. Also, we venture to say that we can tell him with greater accuracy what the result of the operation will be. Finally, if the conclusions based upon this study are correct, our future results should show a distinct improvement.

But we are still lacking information as to what result may be expected in case we do not operate, because, so far as we know, no large group of medically treated cases has been carefully followed over a long period of time. The choice between operating or not upon each patient is, to that

serious degree, made difficult. We are beginning, however, to correct this fault. For the past five years, a Medical Follow-Up Clinic, comparable to the Surgical Follow-Up Clinic, has existed for all the cases treated medically in the wards of the Presbyterian Hospital. While this period of observation is short, it is sufficient to indicate that almost all of the patients so treated become unsatisfactory at some time after leaving the hospital, and that at any given time approximately one-fourth of them are unsatisfactory. These two observations form a basis of comparison, respectively, for the surgical "Results According to Cases" and "Results According to Years." It is not a good basis, because many of the medically treated cases are milder than those operated upon, but it has some value. We do not yet know how many of these patients will die of their ulcers over the years, as a point of comparison with the postoperative and late death rate of the surgically treated patients, but we do know that the medical mortality is a real one, as some of the medically treated cases have already died of hemorrhage or perforation since leaving the hospital. In ignorance of so much that we need to know, we have adopted the policy of considering surgery only for individuals who have not responded favorably to one or more thorough courses of medical regimen including rest in bed. Some day, perhaps, it will be possible to select cases for operation without subjecting them to such courses, which are always prolonged and sometimes futile. From the records of the Medical Follow-Up Clinic, five or ten years from now, may well come information that will enable us to predict which cases are apt to do well under medical treatment and which cases not. Early operation on the latter would save not only time but lives as well, which now are lost by hemorrhages, perforations, or postponement of operation until the disease is associated with serious complications or the patient is debilitated by illness or has reached advanced years.

Another question to consider in appraising the results of any form of therapy for ulcer is: To what degree of freedom from symptoms are we aiming to bring the patients? Are we to be content only with complete freedom from digestive disturbances, or may we be satisfied if they achieve the digestive status of people without ulcers? If the latter, what is that status? In order to gain some answer to the last question, we interviewed 100 patients in the Fracture Follow-Up Clinic, all of whom had been hospitalized for fractures, and whose residence, age and economic level were roughly comparable to those of our ulcer cases. The questions asked of them were the ones asked in the Ulcer Follow-Up Clinic, and the individuals were rated according to their symptoms in the same manner as in the Ulcer Clinic. As a result of an analysis of this study, 81 per cent were classified as satisfactory and 19 per cent as unsatisfactory. In those that had symptoms, worry and fatigue were recognized as the usual predisposing factors. While this study comes far from setting a standard, it does agree with the common knowledge that somewhere around 10 to 20 per cent of people will have

CHART 1.

Serial No. ----

Name Mr. G. P. Age 30 Sex Male Race Negro Unit No. 50154

Address 436 Convent Avenue
Apartment 36
New York City

Religion Prot. Surg. Path. No. -----

Birthplace B.W.I. X-Ray No. 7356

Marital State Married Attending Dr. X

Occupation Porter Surgeon Dr. Y.

Personality Pleasant- well adjusted

Adm. May 9/1921. Dis. May 28/1921

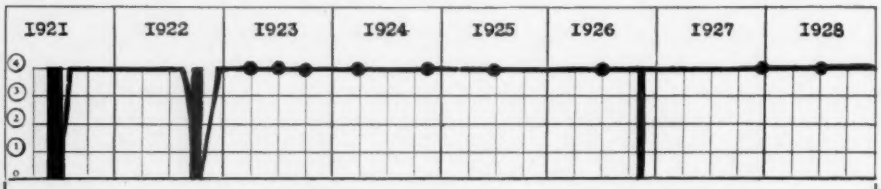
X-Ray Diag. Ulcer of duodenum
Localized tenderness and
50% 6-hr. residue

Remarks Uncomplicated convalescence

Discharge Diag. Ulcer of duodenum

Operation Posterior gastroenterostomy, side of stomach to side of intestine, suture.

CHART 2.



Epi. pain. intermitt. 7 yrs.

Alc. O
Tobacco: 1 plus
Tarry stool
Constipated
X-ray: Duod. U.

G. P. 50154

Pain
X-ray: Duod. ulcer
Crater?
50% retention

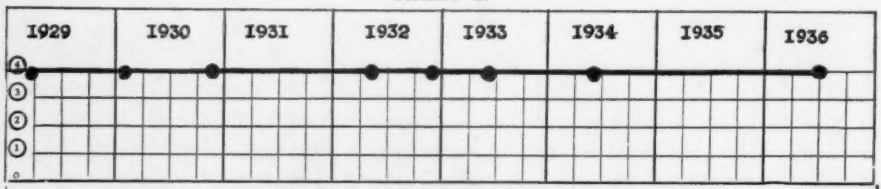
OP. POST G. E.
Scar 1st part duod.

X-ray, post-op. No retention
Free stoma

Lobar pneumonia

Pain 3 plus; Bleeding once. RBC 4 mil, Hgb. 70%.
Obstruction high-grade (X-ray: once large retention, once 50% 6-hr.)

CHART 3.



EXPLANATORY NOTE

Each follow-up visit is represented by a circle —●—, placed at the level of the patient's symptomatic rating at that time.

The continuous rating since the previous follow-up visit is indicated at the proper level by a continuous line.

The heavy perpendicular lines indicate hospitalization.

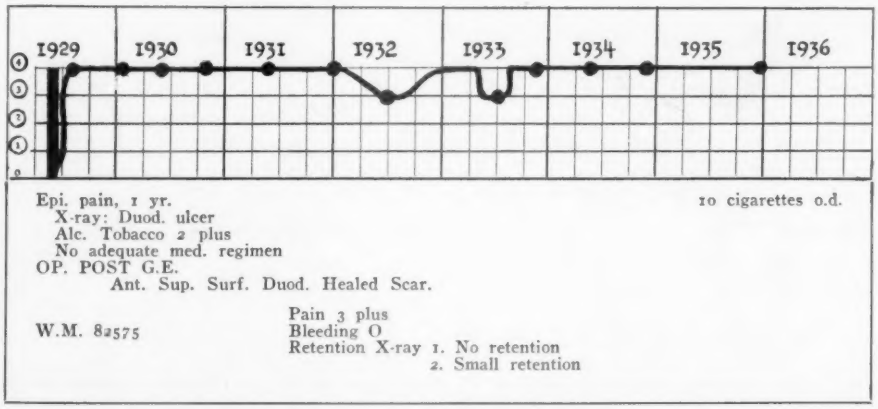
digestive symptoms of more than mild degree without demonstrable ulcers and that from time to time digestive complaints will appear among ulcer patients even if their ulcers are healed.

We are only too well aware of the part played by emotional stress and strain, instability and real psychopathic conditions in this disease, but have lacked the opportunity of studying this phase of the problem as it should be studied. Suffice it to say that this factor colors the results to be reported.

A glance at several illustrative cards will make more clear the type of individual records that form the basis for the summaries printed in the tables. G. P., Charts No. 1, 2 and 3, was treated in the hospital in 1921 for symptoms of duodenal ulcer of seven years' duration. The symptoms recurred a year later, and posterior gastro-enterostomy was performed. He had six-hour retention, roentgenologically, in 1921 (amount not stated), and 50 per cent retention again, in 1922, before operation, with evidence of ulcer at both observations. He also had severe pain and gross bleeding. During almost 14 years of postoperative visits, he has admitted no distress. He is accordingly classed as Duodenal Ulcer with Obstruction and Hemorrhage, posterior gastro-enterostomy, Group 4 in the tables of "Results According to Cases," with 14 Group 4-years in the tables of "Results According to Years."

W. M., Chart 4, illustrates Duodenal Ulcer with Pain, because he had no high-grade persistent obstruction and no gross bleeding. In the "Results According to Cases," he appears as Group 3, because he complained of mild symptoms at a follow-up visit (on two occasions in this instance). In the "Results According to Years," he has four Group 4-years and two Group 3-years to his credit. This case and the one preceding are considered satisfactory, because they have never had severe postoperative symptoms.

CHART 4.



B. F., Charts 5 and 6, represents a Duodenal Ulcer with Pain, who, after three years of pretty constant distress, was treated in the hospital in 1924. He had recurrence of symptoms in 1925, for which Gastro-enterostomy was done. After more than eight years in which he admitted no symptoms, he suffered a severe hemorrhage and recurrence of ulcer pain. He is rated in

Results According to Cases as Group 2, Unsatisfactory, with, however, eight Group 4-years and one Group 1-year in Results According to Years.

CHART 5.

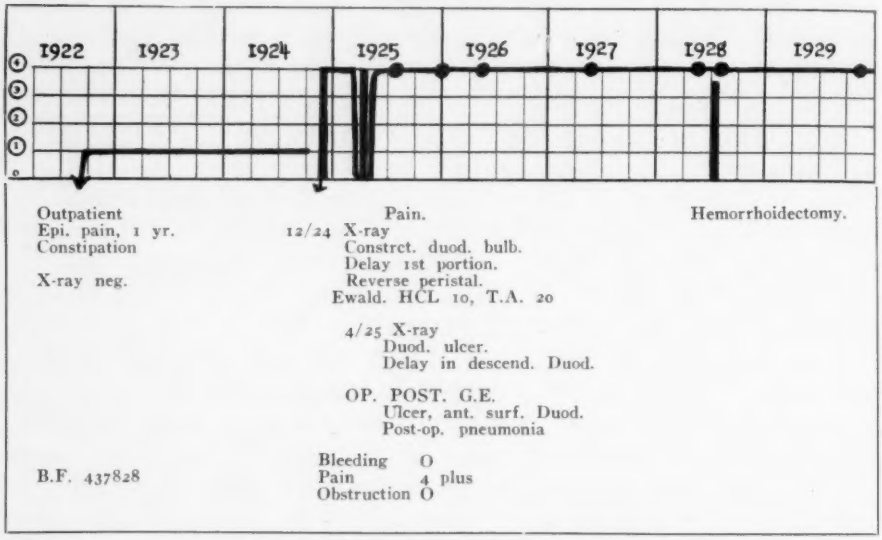
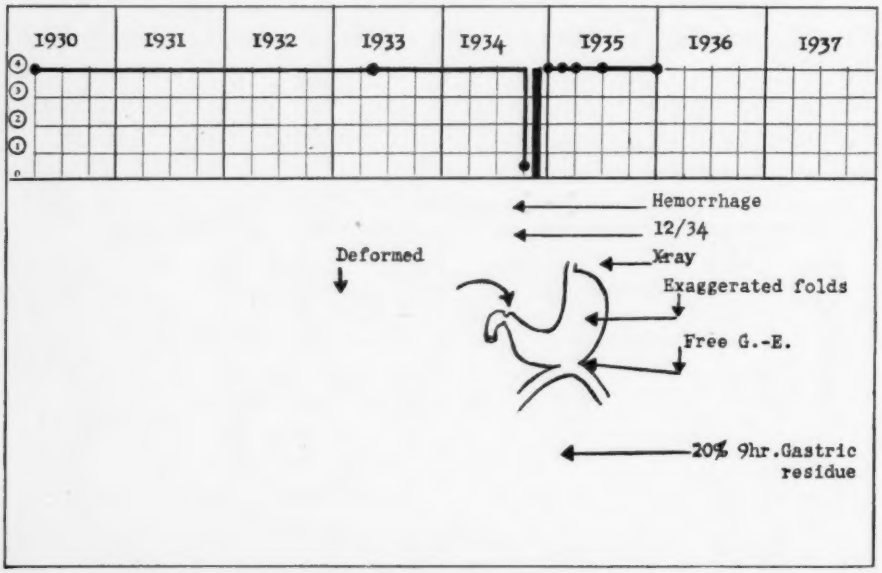
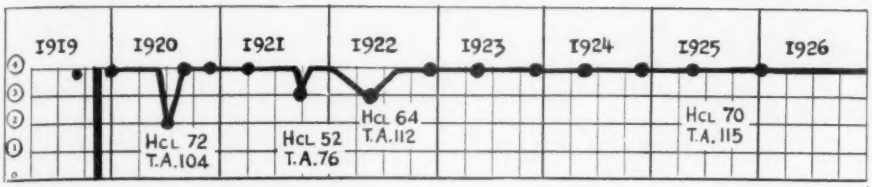


CHART 6.



J. H., Charts 7 and 8, after a Finney type of pyloroplasty, is rated as a Group 1, unsatisfactory, in "Results According to Cases," because of his experiences in 1929 and 1932, although for the first ten years his complaints were few. He has six Group 4-years, four Group 3-years, two Group 2-years and three Group 1-years.

CHART 7.



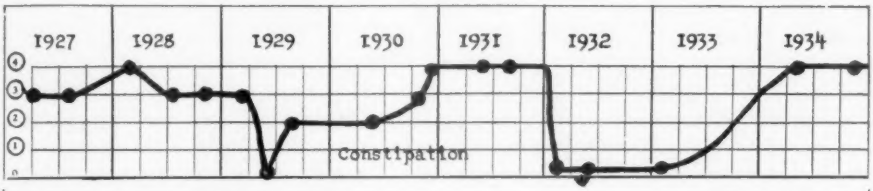
6 mos. epi. pain.

Epi. pain since age 15.
1917, perforated. Gastrorrhaphy Volunteer Hosp.
Well until 6 mos. ago.
No adequate med. regimen.
Very nervous.

X-ray 11/19 Duod. ulcer. Ewald HCL 59, T.A. 82
OPERATION. FINNEY PYLOROPLASTY.
Many adhesions. Induration 2 × 3 cm. prox. to pyloric ring, post. wall.
J.H. 330152

Bleeding O
Pain 4 plus
Retention O

CHART 8.



Occ. alkali

Pain, typ. ulcer.

X-ray 7/29
Irregularities. Duod. cap and prepylorus. No crater.

Veterans' Hosp.

Rest and diet.

Not all cases were so easy to classify as the ones just cited, but the difficult ones were not numerous. Having assembled our information regarding each individual, it was then possible to arrange the cases into groups and so construct the tables. For completeness, these tables include all our cases, and so contain many figures that are not of great significance. Where the figures seem of special interest, they are printed in bold-faced type.

Table I affords a comparison of the results of various operations for duodenal ulcer, according to cases. The gastro-enterostomies are divided into three groups, performed in individuals, who, before operation, had obstruction, hemorrhage or pain. This division is not made for the other operations, because in the partial gastrectomies the difference in results among the three groups is not marked, and in the other operations the number of cases is not large enough to divide. It is to be noted that in the Obstruction group, proportionately about twice as many individuals remained always satisfactory as in the Hemorrhage or Pain groups. This is shown in the column headed "Satisfactory Survivors." It is true that the average follow-up for the Obstruction group is a little shorter, but not enough to account for this striking difference. In the same column, it also appears that the results after partial gastrectomy are far better

TABLE I

DUODENAL ULCER

FOLLOW-UP RESULTS ACCORDING TO CASES

Type of Operation	Total Cases	P. O. Deaths		Insuff. Follow-Up	Followed Survivors	Satisfactory Survivors		Unsatisfactory Survivors		Group 4	Group 3	Group 2	Group 1	Average Follow-Up Years
Post. gastro-enterostomy. Obstruction group	70 (14)*	7 (2)	10% 14%	0	63 (14)	51 (11)	81% 79%	12 (3)	19% 21%	36 (7)	15 (4)	3 (1)	9 (2)	5.4
Post. gastro-enterostomy. Hemorrhage group	46	7	15%	7	32	13	41%	19	59%	8	5	3	16	6.3
Post. gastro-enterostomy. Pain group	109	9	8%	11	89	39	44%	50	56%	22	17	24	26	6.3
Totals	225	23	10%	18	184	103	56%	81	44%	66	37	30	51	
Partial gastrectomy	72	13	18%	4	55	42	76%	13	24%	28	14	7	6	4.3
a. Billroth II 35 Pólya 37														
b. Billroth I 6 Moynihan 3	9	2	22%	0	7	3	43%	4	57%	3	0	3	1	5.0†
Pyloroplasty														
a. Finney type	13	1	8%	2	10	7	70%	3	30%	5	2	2	1	3.3‡
b. Horsley type	11	0		0	11	6	55%	5	45%	4	2	2	3	4.6
Excision or cauterization plus gastro-enterostomy	10	0		1	9	4	44%	5	56%	4	0	2	3	5.0§
Miscellaneous	15	8	53%	2	5	1	20%	4	80%	0	1	2	2	4.8
Totals	355	47		27	281	166		115		110	56	48	67	

* Figures in parentheses refer to the number of bleeders in the obstruction cases.

† Satisfactory cases followed only one year each.

‡ Only two satisfactory cases followed over two years.

§ Three of the four satisfactory survivors were obstruction cases.

TABLE II

DUODENAL ULCER

FOLLOW-UP RESULTS ACCORDING TO YEARS

Type of Operation	Total Years	Satisfactory Years		Unsatisfactory Years		Symptomatic Group				Deaths from Ulcer	Deaths from Other Causes
						Four	Three	Two	One		
						Yrs.	Yrs.	Yrs.	Yrs.		
Post. gastro-enterostomy. Obstruction group	346	314	91%	32	9%	277	37	12	20	1	6
Post. gastro-enterostomy. Hemorrhage group	201	161	80%	40	20%	108	53	11	29	2	4*
Post. gastro-enterostomy. Pain group	575	438	76%	137	24%	311	127	46	91	1	8
Totals	1,122	913	81%	209	19%	696	217	69	140	4	18
Partial gastrectomy											
a. Billroth II and Pólya types	230	195	85%	35	15%	168	27	19	16	1	3
b. Billroth I and Moynihan	35	27	77%	8	23%	22	5	4	4	0	1*
Pyloroplasty											
a. Finney type	33	28	85%	5	15%	20	8	1	4	0	0
b. Horsley type	46	39	85%	7	15%	24	15	2	5	0	0
Excision or cauterization of ulcer plus gastro-enterostomy	45	32	71%	13	29%	29	3	5	8	1	0
Miscellaneous	24	14	68%	10	32%	5	9	4	6	1	0
Totals	1,535	1,248		287		964	284	104	183	7	22

* One from lung condition developing postoperative.

than after gastro-enterostomy when the latter is performed for hemorrhage or pain. For the Obstruction group alone, partial gastrectomy has given no better results than gastro-enterostomy, and the death rate for the latter is less. The Finney type of pyloroplasty has the third best results, but this statement is made with the important reservation that only two of the seven satisfactory cases in this group have been followed for more than two years. The death rates are discussed below.

Table II gives the same comparison as Table I, but based on follow-up-years instead of cases. In this table, each year is counted at the lowest symptomatic rating to which the patient fell at any time during that year. The results of gastro-enterostomy performed for the Obstruction group again lead, with only 9 per cent-years that contained at any time an unsatisfactory rating. Partial gastrectomy of the Billroth II or Pólya types yielded 85 per cent satisfactory-years, better than gastro-enterostomies as a whole, but not so good as the gastro-enterostomies in the Obstruction group. The pyloroplasties also yielded 85 per cent satisfactory-years, but their total number of follow-up-years is small. The results in this table, therefore, parallel those in Table I. The difference between the two ways of judging the results appears in this fact: In Table I, only 59.1 per cent of all the cases remained satisfactory; whereas, in Table II, 81.3 per cent of all the follow-up-years were satisfactory.

In Table II also appears the interesting fact that seven of the 281 individuals that were followed died of their ulcer at some time after leaving the hospital. To these must be added two, who died of pulmonary lesions which developed shortly after operation, one of pulmonary tuberculosis which became active, and one of multiple lung abscesses. Twenty died of other causes.

Table III and Table IV give the same results as Tables I and II, but in relation to gastric ulcer instead of to duodenal ulcer. There is no question but that for gastric ulcer, partial gastrectomy of the Billroth II or Pólya types has been the procedure of choice, with 90 per cent of the survivors satisfactory when grouped according to cases (Table III), and 92 per cent satisfactory-years (Table IV). Few major surgical procedures for any lesion would have so good a record. The postoperative death rates are discussed below. Gastro-enterostomies as a group did poorly. Four of the 70 followed survivors in the entire gastric group died of their ulcer after leaving the hospital. Of these deaths, three occurred among the 13 gastro-enterostomies. From these results, it is plain that gastro-enterostomy for gastric ulcer is contraindicated, but that an adequate partial gastrectomy offers real hope of cure. Actually, only two of the 31 followed survivors of partial gastrectomy have had recurrence of ulcer symptoms, as one of the three listed as unsatisfactory was so classified because he died of pulmonary tuberculosis activated by the operation.

TABLE III

GASTRIC ULCER

FOLLOW-UP RESULTS ACCORDING TO CASES

Type of Operation	Total Cases	Postop. Deaths	Insuff. Follow-Up	Followed Survivors	Satisfactory Survivors		Unsatisfactory Survivors		Group 4	Group 3	Group 2	Group 1	Average Follow-Up
Partial gastrectomy													
a. Billroth II and Pólya	37	3	3	31	28	90%	3*	10%	20	8	1	2	5.9
b. Sleeve 13 Billroth I 1 Moynihan 1	15	4	0	11	5	45%	6	55%	0	5	3	3	6.2
Posterior gastro-enter.	13	0	0	13	3	23%	10	77%	3	0	4	6	3.5
Excisions 9 Cauterizations 4 Pyloroplasties 3	16	2†	4	10	7	70%	3‡	30%	3	4	0	3	4.8
Miscellaneous	7	2	0	5	2	40%	3	60%	0	2	2	1	5.7
Totals	88	11	7	70	45		25		26	19	10	15	

* One Tbc. death. † Both deaths in excisions. ‡ Unsatisfactory: 2 pyloroplasties; 1 excision.

TABLE IV

GASTRIC ULCER

FOLLOW-UP RESULTS ACCORDING TO YEARS

Type of Operation	Total Years	Satisfactory Years		Unsatisfactory Years		Symptomatic Group: Four	Three	Two	One	Deaths from Ulcer	Deaths from Other Causes
Partial gastrectomy											
a. Billroth II and Pólya	219	203	92%	16	8%	172	31	10	6	0	9*
b. Sleeve, Billroth I and Moynihan	93	74	80%	19	20%	48	26	12	7	1	0
Posterior gastro-enter.	46	19	41%	27	59%	11	8	16	11	3	2
Excisions Cauterizations Pyloroplasties	76	60	79%	16	21%	46	14	7	9	0	0
Miscellaneous	40	33	83%	7	17%	5	28	1	6	0	0
Totals	474	389		85		282	107	46	39	4	11

* One death from tuberculosis.

TABLE V

RESULTS ACCORDING TO CASES

DUODENAL ULCER

	Satisfactory	Unsatisfactory	Satisfactory but Not Followed For Period Indicated	Became Unsatisfactory During Period Indicated
a. Gastro-enterostomy for obstruction				
At 3 yrs. postop.	40	6	17	6
At 5 yrs. "	29	10	24	4
At 10 yrs. "	11	11	41	1
At 15 yrs. "	4	12	47	1
b. Gastro-enterostomy for bleeding				
At 3 yrs. postop.	17	10	5	10
At 5 yrs. "	10	14	8	4
At 10 yrs. "	5	18	9	4
At 15 yrs. "	1	19	12	1
c. Gastro-enterostomy for pain				
At 3 yrs. postop.	46	35	8	35
At 5 yrs. "	34	40	15	5
At 10 yrs. "	13	46	30	6
At 15 yrs. "	4	49	36	3
d. Total gastro-enterostomy				
At 3 yrs. postop.	103	51	30	51
At 5 yrs. "	73	64	47	13
At 10 yrs. "	29	75	80	11
At 15 yrs. "	9	80	95	5
e. Partial gastrectomy for duodenal and pyloric ulcers (Billroth II and Pólya types)				
At 3 yrs. postop.	29	9	17	9
At 5 yrs. "	24	11	20	2
At 10 yrs. "	13	13	29	2
At 15 yrs. "	3	13	39	0
f. Pyloroplasty for duodenal and pyloric ulcers Horsley type: 11 cases Finney type: 10 cases				
At 3 yrs. postop.	8	8	5	8
At 5 yrs. "	2	9	10	1
At 10 yrs. "	1	9	11	0
At 15 yrs. "	0	9	12	0
GASTRIC ULCER				
a. Partial gastrectomy (Billroth II and Pólya types)				
At 3 yrs. postop.	22	2	7	2
At 5 yrs. "	18	2	11	0
At 10 yrs. "	11	2	18	0
At 15 yrs. "	2	3	26	1
b. Pyloroplasties, excisions, cauterizations				
At 3 yrs. postop.	6	2	2	2
At 5 yrs. "	4	3	3	1
At 10 yrs. "	2	4	4	1
At 15 yrs. "	0	4	6	0
c. Posterior gastro-enterostomy				
At 3 yrs. postop.	2	9	2	9
At 5 yrs. "	1	9	3	0
At 10 yrs. "	0	10	3	1
At 15 yrs. "	0	10	3	0

It is interesting to know how many individuals remained free of symptoms three, five, ten, and fifteen years after operation. Table V gives this information. In addition, it also shows the number of individuals who experienced their first recurrence of symptoms in each of the four given periods, *i.e.*, in the first three years, between the third and fifth, and fifth and tenth, and the tenth and fifteenth years. It is a table compiled according to cases, that is, once an individual became unsatisfactory, even temporarily, he was thereafter classed as unsatisfactory. In the first group tabulated, the cases of duodenal ulcer with obstruction treated by gastro-enterostomy, it is seen that the 53 cases comprising this group were distributed as follows: After three years, 40 were still satisfactory, six had become unsatisfactory, and 17 were not yet followed for three years, but so far as they had gone were still satisfactory. At five years, four more had become unsatisfactory, so that the alignment then was 29 satisfactory, ten unsatisfactory, and 24 satisfactory but not followed the full five years. And so on for the tenth and fifteenth years. The results for the other groups of cases and after other operations may be similarly read. It is a difficult chart from which to draw deductions, because so many of the cases have not been followed for the full ten- or 15-year periods. It demonstrates, however, that a distressing number of initial recurrences of symptoms appear many years after operation. Of 29 cases free of symptoms after gastro-enterostomy for ten years, five had recurrences later, *i.e.*, before 15 years. In the face of this, the publication of three-or five-year "cures" becomes meaningless.

Table VI has to do with the same cases included in Table V, but presents their postoperative records from the point of view of years instead of cases. It shows the number and proportion of the cases that were satisfactory during each postoperative year. This table, therefore, takes account of the good years and the bad years equally, without regard to how many years after operation the symptoms first recurred, or how many individuals remained free of symptoms for their whole postoperative course. The maze of numbers contained in the table is at first sight confusing, perhaps, but if the eye is allowed to travel down each column headed "Satis. Cases," the main significance of the figures becomes apparent. In the first place, it is interesting how little variation there is in any group in the proportion of cases who are free of symptoms in the various postoperative years. Secondly, it is seen that, among the groups, the obstruction cases with gastro-enterostomy (first group on the left-hand side) are almost uniformly over 90 per cent free of symptoms. The other groups are doing less well in almost every year. The difference becomes more striking if the columns showing "Unsat. Cases" are compared. In the years where the number of cases is small, the percentages lose meaning.

The findings in Tables V and VI agree in general with those in Tables I to IV, so far as the results of the various operations are concerned. Gastro-enterostomy for the obstruction cases has the best record, with partial gas-

TABLE VI

RESULTS BY YEARS

DUODENAL ULCER

Yrs. P. O.	Posterior Gastro-enterostomy for								Total Gastro-enterostomy				Partial Gastrectomy, Billroth II and Pólya				Pyloroplasties			
	Obstruction				Hemorrhage				Pain											
	Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases	
1	58	94%	4	6%	28	88%	4	12%	68	76%	22	24%	154	84%	30	16%	40	87%	6	13%	15	71%	6	29%
2	46	94%	3	6%	21	81%	5	19%	53	68%	25	32%	120	78%	33	22%	25	83%	5	17%	12	80%	3	20%
3	36	95%	2	5%	19	83%	4	17%	55	78%	16	22%	110	83%	22	17%	23	88%	3	12%	11	92%	1	8%
4	31	91%	3	9%	15	71%	6	29%	48	79%	13	21%	94	81%	22	19%	21	84%	4	16%	7	88%	1	12%
5	26	87%	4	13%	12	71%	5	29%	43	83%	9	17%	81	82%	18	18%	20	91%	2	9%	5	100%	0	
6	23	92%	2	8%	11	85%	2	15%	32	76%	10	24%	66	83%	14	17%	17	81%	4	19%	5	100%	0	
7	21	100%	0		8	67%	4	33%	28	80%	7	20%	57	84%	11	16%	16	84%	3	16%	4	80%	1	20%
8	18	100%	0		7	64%	4	36%	25	74%	9	26%	50	79%	13	21%	12	80%	3	20%	3	100%	0	
9	12	80%	3	20%	7	78%	2	22%	26	81%	6	19%	45	80%	11	20%	12	92%	1	8%	2	100%	0	
10	10	91%	1	9%	4	67%	2	33%	21	81%	5	19%	35	81%	8	19%	8	100%	0		2	100%	0	
11	7	100%	0		4	67%	2	33%	14	74%	5	26%	25	78%	7	22%	4	80%	1	20%	0		0	
12	7	100%	0		6	100%	0		6	55%	5	45%	19	80%	5	20%	0		2		0		0	
13	7	100%	0		5	100%	0		5	63%	3	37%	17	85%	3	50%	1	50%	1	50%	0		0	
14	4	80%	1	20%	4	100%	0		6	86%	1	14%	14	88%	2	12%	0		0		0		0	
15	3	75%	1	25%	4	100%	0		3	75%	1	25%	10	83%	2	17%	0		0		0		0	

trectomy almost equally good. The pyloroplasties, having so few cases, are difficult to judge, but do not seem to do as well as following the operations just mentioned. In reading these two tables it is helpful to bear in mind that so far as the study of the results of medical treatment has gone, it seems to show that: First, very few medically treated cases have gone five years without recurrence of symptoms (compare with Table V); and, second, in any year after hospitalization, approximately 75 per cent of the cases are free of symptoms, *i.e.*, satisfactory, and 25 per cent are having symptoms (compare with Table VI).

A study of the status of the postoperative patients according to calendar years, instead of postoperative-years, is not tabulated here. It brought out only one fact of interest, namely, that the proportion of individuals free of symptoms from year to year remained nearly constant. We could show no increase in symptoms in the group as a whole during the depression years, although we were impressed in the Follow-Up Clinic by the apparently close relation in certain individuals between increased economic stress and recurrence of ulcer symptoms.

TABLE VI (a)

RESULTS BY YEARS

GASTRIC ULCER

Yrs. P. O.	Partial Gastrectomy, Billroth II and Pólya				Excisions, Cauterizations, Pyloroplasties				Posterior Gastro-enterostomy			
	Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases		Satis. Cases		Unsat. Cases	
1	28	88%	4	12%	7	70%	3	30%	9	79%	4	21%
2	25	96%	1	4%	9	90%	1	10%	5	50%	5	50%
3	23	96%	1	4%	7	88%	1	12%	2	29%	5	71%
4	22	95%	1	5%	7	88%	1	12%	1	20%	4	80%
5	18	100%	0		5	83%	1	17%	1	25%	3	75%
6	15	100%	0		5	100%	0		1	33%	2	67%
7	14	100%	0		4	80%	1	20%	0		2	100%
8	13	100%	0		3	100%	0		0		2	100%
9	11	100%	0		3	75%	1	25%	0		0	
10	11	100%	0		2	50%	2	50%	0		0	
11	6	86%	1	14%	2	67%	1	33%	0		0	
12	5	83%	1	17%	3	100%	0		0		0	
13	4	80%	1	20%	2	67%	1	33%	0		0	
14	3	75%	1	25%	0		1	100%	0		0	
15	2	67%	1	33%	1	100%	0		0		0	

Table VI (a) shows the "Results by Years" in gastric ulcer, just as Table VI shows them in duodenal ulcer. The points of interest in this table are the excellent record of the partial gastrectomies and the very poor record of the gastro-enterostomies.

TABLE VII

SUMMARY OF UNSATISFACTORY RESULTS

DUODENAL AND GASTRIC ULCERS

Type of Operation	Unsatisfactory Cases	Poorly Functioning Gastroent.	Hemorrhage	Recurrent Ulcer	Marginal Ulcer	Jejunal Ulcer	Total Ulcers	Retention	Spastic Jejunum	Neurosis	Reoperation	Died of Ulcer During Follow-Up
Gastro-enterostomy. Obstruction group	12	6	6	4	3	2	9	4	0	1	3	1
Gastro-enterostomy. Hemorrhage group	19	1	11	2	2	1	5	1	0	1	3	2
Gastro-enterostomy. Pain group	50	16	13	10	14	2	26	9	2	3	11	1
Totals	81	23	30	16	19	5	40	14	2	5	17	4
Partial Gastrectomy Billroth II and Pólya Duodenal ulcer	13	1	4	1	4	2	7	1	0	0	2	1
Partial Gastrectomy Billroth II and Pólya Gastric ulcer	3	1	1	0	0	1	1	0	0	0	0	0
Pyloroplasty Duodenal ulcer	8	0	4	3	0	0	3	2	0	0	1	0
Pyloroplasty Gastric ulcer	3	0	2	0	0	1	1	0	0	0	0	0
Post. gastro-enter. Gastric ulcer	10	0	5	0	0	0	0	0	0	0	0	3

In Table VII an attempt is made to analyze the causes of failures occurring after the operations that were performed most frequently. A total of 314 individuals were followed after these operations, of which 118 sooner or later became, temporarily at least, unsatisfactory. This table was arranged in order to show whether any one procedure was especially prone to be followed by any single cause of failure. Pain is not included in this table as it occurred in nearly all these patients, whatever their operation. It does not appear from this record that there is any undesirable result which occurs after one type of operation more than after another. Hemorrhage occurred among the unsuccessful cases after all operations in not very different proportion. It occurred regardless of whether the patient had bled before operation or not. Recurrent, marginal or jejunal ulcers, demonstrated chiefly by roentgenologic evidence, appeared in about half the unsuccessful gastro-enterostomies and half the unsuccessful partial gastrectomies. Poorly functioning stomas appeared relatively more frequently among the gastro-enterostomies. Neuroses, so diagnosed by a psychiatrist, are found in only five cases, but this figure is probably lower than it would be if adequate psychiatric examination were possible for all the patients. Certainly this is a complication that should be recognized, if possible, before operation is undertaken, as few of these individuals are subjects for surgery.

The number of wholly unsuccessful cases, compared with those who had only temporary or mild recurrences, may also be estimated from this table. In the two right-hand columns appear the number of individuals that were subjected to secondary operations because of the severity of their recurrences, and the number that died of their ulcers. Among the 118 patients, there were 20 secondary operations, of which six were partial gastrectomies after unsuccessful gastro-enterostomies, six were closures of gastro-enterostomy stomas, and the remainder were miscellaneous procedures. It is interesting that only two of these operations were for acute perforations. Of the eight deaths, four were attributed to hemorrhage, two occurred after secondary operations, one followed the development of carcinoma at the site of an old gastric ulcer, and one is unclassified.

The question of how often carcinoma develops in previously benign gastric ulcers is not in any way answered by our data. Among a total of 88 gastric ulcers, we have observed three die of gastric carcinoma, but we do not know that these three did not have carcinoma at the time they first developed symptoms. We have included them among the ulcers because none of them was recognized to have carcinoma in less than five years after the recognition of the ulcer. Other cases with carcinoma have been placed with the carcinoma group, whatever the diagnosis made at the time of operation. The point of practical importance in this matter is the recognition of the difficulty of distinguishing between the benign and malignant ulcers in the stomach even at operation. With the good results that have come of partial resections for benign ulcers, we are more encouraged than ever to resect doubtful cases that do not heal rapidly under medical care.

TABLE VIII

POSTERIOR GASTRO-ENTEROSTOMY FOR DUODENAL ULCER

CHIEF CAUSES OF DEATH

Pneumonia	7
*Hemorrhage	7
Peritonitis	2
Ileus	1
Dilated stomach	1
Pulmonary embolus	1
Miliary tuberculosis	1
During operation	1
Inanition	1
Lung abscess	1
Total	23

Autopsies 13—57%

*2 from ulcer bed.
2 from undetermined source.
2 from G.E. suture line.
1 from abdominal wall.

The postoperative death rates shown in Table I and II are higher than most of those which have been published. Table VIII gives the chief causes of death after gastro-enterostomy for duodenal ulcer. Over half of these cases were autopsied. Pneumonia appeared to be the chief cause in approximately one-third of the cases. Hemorrhage was the chief cause in another third. It is to be noted that at least two of the fatal hemorrhages occurred from the ulcer bed. Whether these two would have occurred without operation is impossible to tell. But this table affords a poor explanation of why so many died.

TABLE VIII (a)

POSTERIOR GASTRO-ENTEROSTOMY FOR DUODENAL ULCER

MORTALITY ACCORDING TO AGE

Age Years	No. of Cases	P.O. Deaths	Death Rate
11–20	7	0	0
21–30	31	0	
31–40	73	6	7.1%
41–50	54	3	
51–60	44	9	23.3%
61–70	15	4	
71–80	1	1	
	225	23	10.2%

Table VIII (a) is perhaps more significant, showing how the mortality rate rose with the age of the patients operated upon. Under 30, there were no deaths, between 30 and 50, there were nine deaths among 127 patients (7.1 per cent), but in patients over 50 the death rate was 23.3 per cent. Another factor, that we cannot appraise accurately, is the condition of the patients before operation, irrespective of age. About one-third of those that died were in poor condition before operation, due to hemorrhages, too prolonged medical regimen without improvement, or other causes. In the earlier years of this study, prolonged dehydration before operation was not uncommon. It is clear from these considerations that the operative risk in gastro-enterostomy cannot be stated for any individual in terms of the average, as is true in most operations.

TABLE VIII (b)

POSTERIOR GASTRO-ENTEROSTOMY FOR DUODENAL ULCER

MORTALITY BY FIVE-YEAR PERIODS

Years	Total No. of Cases	Postop. Deaths		Survivors	
1916–1920	32	4	12.5%	28	87.5%
1921–1925	60	9	15%	51	85%
1926–1930	60	5	8.3%	55	91.7%
1931–1935	70	5	7.1%	65	92.9%

Table VIII (b) shows that the postoperative mortality of gastro-enterostomy has fallen during the last decade to about half of what it was during the previous decade. So many factors seem to have contributed to this drop that we have not attempted to analyze them.

The mortality rate in partial gastrectomies has been even more of a problem than in gastro-enterostomies. In all types of partial gastrectomy, there were 22 deaths in 133 cases, a mortality rate of 16.5 per cent. In duodenal ulcers the rate was 18.5 per cent; in gastric ulcers 13 per cent. Table IX gives an analysis of the chief causes of death in the two types of partial gastrectomy most often performed, namely, the Billroth II and Pólya types. It is not easy even at autopsy to assign a chief cause of death in several of these cases. They died with multiple lesions. But Table IX is wholly clear as to the importance of one item, namely, peritonitis from leakage of the duodenal stump. At least six of the 16 fatalities were traceable to this cause, and there is little doubt that some of the three labeled "Uncertain" and the two labeled "Peritonitis of Unknown Source" could be added to this number. So that somewhere between 37.5 and 68.8 per cent of our deaths are attributable to leakage! Of perhaps even greater importance is the item of obstruction, which we know occurred in nine of the 16 fatalities and may have been present in five more. By obstruction we refer to kinks or twists occurring close to the site of anastomosis in either the proximal or distal jejunal loops.

Four of the six proven leaking duodenal stumps were associated with, and probably partly caused by, such obstructions. A reduction of mortality must obviously await control of these two complications.

TABLE IX

PARTIAL GASTRECTOMY FOR DUODENAL AND GASTRIC ULCER

		P.O.	Deaths	Autopsies
Billroth II	54	8	14.8%	2
Pólya type	55	8	14.8%	7
Totals	109	16		9

CHIEF CAUSES OF DEATH

	Bill. II	Pólya	Total
Uncertain	3	0	3
Peritonitis, unknown source	2	0	2
Hemorrhage	1	1	2
Leakage of duodenal stump	2*	4†	6
Obstruction alone	0	3	3
Totals	8	8	16

* 1 also had obstruction.
† 3 also had obstruction.

TABLE IX (a)

PARTIAL GASTRECTOMY

Complications, Not Fatal, but Requiring Second Operation

	Bill. II	Pólya	Total
Peritonitis, unknown source	1		1
Atonic stomach	1		1
Leakage of duodenal stump	0	2	2
Obstruction alone	0	5*	5*
Totals	2	7	9

* One of these after 16 months.

TABLE IX (b)

PARTIAL GASTRECTOMY

Serious Complications

Atonic stomach	1
Hemorrhage	2
Peritonitis, unknown source	3
Uncertain nature	3
Leakage of duodenal stump (of which 4 had obstruction also)	8
Obstruction alone	8
Total	25

In addition to the complications which ended in death, there were, in other individuals, complications which required operative interference to save life early during the postoperative course. These are listed in Table IX (a), and here again appear leakage of the duodenal stump in two of the nine cases, and obstruction in five. (One of these obstructions was evident shortly after operation but was incomplete and did not necessitate immediate relief.) A summary of the serious complications, some of which resulted in death, is given in Table IX (b), combining the figures in the two preceding tables. For emphasis, attention is again drawn to the frequency of leaking duodenal stumps and obstruction.

The question immediately comes to mind: How to control these two complications? For the leaking duodenal stump, a drain placed near to the site of the stump, almost as a routine measure, should usually suffice. Not one of the surgeons who operated upon the eight cases that leaked thought that his closure of the stump was insecure, or he would have drained. One cannot predict which of the stumps will yield to the pressure caused by unexpected obstruction, even temporary, or to some other circumstance. Therefore we drain. In several cases where the closure was recognized to be faulty, a drain was employed. Some of these cases developed fistulae, but not one has died. The fistulae, incidentally, have all closed spontaneously, as would be expected provided there were no obstruction to the flow of duodenal contents down the intestine.

As regards the second complication, obstruction, no such simple remedy suggests itself. The obstructions have occurred in either the proximal or distal anastomosing loop of intestine. They have occurred from twists, kinks or constrictions and as the result of edema. Some were brought about by adhesions, some by constriction by the transverse mesocolon when it happened to slip down from the stomach and encircle the anastomosed jejunal loop. It is true that obstructions appear to have occurred much more frequently after the Pólya type of operation than after the Billroth II type (Table X).

TABLE X

POSTOPERATIVE OBSTRUCTION

Proximal Loop	
Anterior Pólya (without entero-enterostomy)	3
Posterior Pólya (without entero-enterostomy)	1
Posterior Pólya (with entero-enterostomy)	2
Billroth II	0
Distal Loop	
Anterior Pólya (without entero-enterostomy)	2
Posterior Pólya (without entero-enterostomy)	1
Posterior Pólya (with entero-enterostomy)	2
Billroth II	1
At Site of Anastomosis	
Billroth I	1

It would seem from analyzing the statistics in Table X, that the answer was to abandon Pólyas and adopt the Billroth II, since the follow-up results were almost equally good. But it is to be recalled that the death rates in the two operations were the same. Seven of the eight deaths after Pólyas were followed by autopsy, but only two of the eight deaths after Billroth II. Therefore, we do not know that the Billroth II operation leads as infrequently to obstruction as we think it does, and see little in our results to make us recommend it over the Pólya.

TABLE XI

PARTIAL GASTRECTOMY FOR PEPTIC ULCER

Operation	Total No. of Cases	Mortality	Followed Survivors	Followed Survivors Satisfactory	Postoperative Complications: Obstruction	Postoperative Complications: Peritonitis
Billroth II	54	8 15%	41	32 78%	1 2%	5 9%
Pólya	55	8 15%	45	38 84%	11 20%	6 11%
a. Ant. Pólya	26	4 15%	21	16 77%	5 20%	4 15%
b. Post. Pólya	29	4 15%	24	22 92%	6 21%	2 7%
x. Pólya with ent.-ent.	19	4 21%	14	12 86%	4 21%	3 16%
y. Pólya without ent.-ent.	36	4 11%	31	26 84%	7 19%	3 8%
Billroth I	7	1 14%	6	4 67%	1 14%	0 0
Moynihan	4	2 50%	2	0 0	0 0	1 25%
Sleeve	13	3 23%	10	4 40%	0 0	1 8%

In Gastric Ulcers:

Of 16 Pólyas followed, 15 were satisfactory.
Of 15 Billroth II followed, 13 were satisfactory.
Of 31 Pólyas and Billroth II followed, 28 were satisfactory, or 90.3%.

In Duodenal Ulcers:

Of 29 Pólyas followed, 23 were satisfactory.
Of 26 Billroth II followed, 19 were satisfactory.
Of 55 Pólyas and Billroth II followed, 42 were satisfactory, or 76.4%.

The final part of this study deals with three matters: First, a comparison of the results after anterior Pólya as compared to posterior Pólya; second, of Pólya with entero-enterostomy as compared to Pólya without entero-enterostomy; and third, the results after Pólya and Billroth II procedures compared with the results after the other types of partial gastrectomy which have been performed. On analyzing the statistics in Table XI, it is seen that there is little to choose between anterior and posterior Pólya from the standpoint of postoperative mortality, follow-up results, or incidence of post-operative complications. The same is true in comparing the Pólya with entero-enterostomy to those without entero-enterostomy. The posterior Pólya has been followed by more satisfactory survivors, proportionately, than has the anterior Pólya, but this difference is explained by the fact that posterior pro-

cedures happened to be done more frequently in the gastric ulcers, in which the results were good whichever of the two procedures was performed. It is interesting that the presence of an entero-enterostomy does not appear to lower the incidence of postoperative obstruction.

With regard to the partial gastrectomies other than Pólya or Billroth II types, the column showing "Followed Survivors Satisfactory" in Table XI explains why the Billroth I, Moynihan and sleeve resection types of procedures are now rarely performed. Few, in our experience, have been followed by satisfactory results. The postoperative death rate after the Moynihan and sleeve resections has been high. It is true, however, that we have performed the Moynihan operation only four times.

Of pyloroplasty, in our experience, not much is to be said. The series is small, 27 in all, of which three were performed for gastric ulcer and the remainder for duodenal ulcer. What little difference can be demonstrated between the Finney and Horsley types is in favor of the former. Tables I and II show the results in the duodenal ulcers. They are encouraging when compared to the results of other procedures, especially as regards the low death rate, but the follow-up is not yet long enough to judge. In the Horsley type, followed for an average of 4.6 years, five out of 11 cases are already unsatisfactory. Only two of the Finney type have remained satisfactory for more than two years, although five others are still free of symptoms, followed for less than two years. The percentage of time free of symptoms after both operations has been good and there has been no death from ulcer after leaving the hospital. None of the other procedures, comprising the smaller groups, holds promise.

CONCLUSIONS

(1) Cases of peptic ulcer should be given the benefit of the safest known treatment first, namely, medical or conservative therapy.

Its definite limitations in certain resistant cases, however, or in the presence of repeated or persistent serious complications, should be recognized. Obstruction, uncontrolled erosion, with or without perforations and hemorrhage, are among the most formidable of these. Cancer in gastric ulcer must always be borne in mind.

A careful study of each patient before operation is the most valuable guide in selecting the proper surgical procedure. This statement does not minimize the importance of the findings at operation.

(2) Despite the present radical trend in surgery, there is a very definite field for gastro-enterostomy in the treatment of this disease; in fact, in cases with persistent obstruction of high grade, it is followed by as satisfactory results as is any other form of surgery. It presents less risk to the patient than more radical procedures.

(3) Subtotal gastrectomy is indicated in pyloric or duodenal ulcer in which persistent pain or recurrent hemorrhage is outstanding. Gastro-enterostomy in these cases has proven unsatisfactory.

(4) Cases of chronic gastric ulcers of the lesser curvature with persistent symptoms of a serious nature respond best to subtotal gastrectomy.

(5) Subtotal gastrectomy is a more formidable procedure than gastroenterostomy and, therefore, will be associated inevitably with a higher postoperative mortality. Its present operative mortality can be lowered by a fuller realization of the actual causes of death.

(6) The material is not available in this clinic for a reasonable study of the results of the various forms of pyloroplasty.

(7) It is obvious that study of peptic ulcer should be directed toward etiology, but until the cause is known, effort should be directed not toward more radical surgery, as is the present trend, but rather toward selective surgery. This selection can be made best only if follow-up results are known.

As surgeons, it is our responsibility to select the patient for operation and the operation for the patient.

CARCINOMA OF THE PERIPAPILLARY PORTION OF THE DUODENUM

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PART ONE

THIS is our third communication dealing with the subject of duodenal carcinoma, the two previous papers being devoted to a consideration of this lesion as it occurs in the suprapapillary portion (Stewart and Lieber) and infrapapillary portion (Lieber, Stewart and Lund) of this short segment of the small intestine. An analysis of carcinoma of the peripapillary portion of the duodenum appears justified in view of the fact that a comprehensive picture of the morbid anatomic and clinical aspects of the disease is lacking, and only slight notice has been given to it in current clinical, surgical and neoplastic treatises.

The papilla of Vater is a small but complex structure with variable anatomic relationships. It is covered superficially with intestinal mucous membrane and it receives the common bile duct and main pancreatic duct, which occasionally unite to form a true ampulla within the papilla proper. We shall cite from our own material and from the literature to show that cancer can arise from the epithelial lining of any of these structures. These tumors, however, early permeate the surrounding tissues and by extension soon involve adjacent structures and so obscure the exact point of origin of the neoplasm. Under these circumstances, which obtained in the majority of cases, there is no way of identifying exactly the structure giving rise to the growth. It is then only possible to classify each case on the basis of the extent of involvement at the time of examination either at operation or autopsy. We incline to the belief, at least with regard to certain of our own cases, that, had the postmortem examination been more painstaking, the gross exploration carried out more diligently, and the tissue blocks for microscopic study selected more judiciously, a greater refinement of classification would be possible. Moreover, the terms ampulla of Vater and papilla of Vater are frequently used interchangeably in many protocols, as though they were synonymous words capable of indicating the same anatomic structure.

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The cases of carcinoma of the peripapillary portion of the duodenum in this series may be classified as follows: (I) Primary carcinoma of the ampulla of Vater. (II) Primary carcinoma of the terminal duct of Wirsung. (III) Primary carcinoma of the terminal common bile duct. (IV) Primary carcinoma of the intestinal mucous membrane covering the papilla of Vater. (V) Carcinoma involving all the epithelial structures of the papilla of Vater under Groups I, II, III and IV. (VI) Carcinoma involving all the epithelial structures comprising the papilla of Vater exclusive of the intestinal mucous membrane.

We propose to present here an analysis of certain features of carcinoma of the peripapillary region of the duodenum and to report 17 new cases of this condition. An attempt was made to collect all the cases reported in the literature, but a few were not available and others undoubtedly escaped our notice, especially where reported in monographs, old systems, obscure journals or under misleading titles. Since many histories were incomplete, inaccuracies and omissions existed in other data, and standards of observation and interpretation were lacking, the numerical sum of the analyses of given clinical or pathologic features does not always equal the total number of cases under consideration.

Three hundred ninety-nine cases were abstracted from the literature. There are included in this study, however, only those cases which have a history, physical findings and gross and microscopic studies of the primary lesion. On this basis, 205 were analyzed, to which are added the 17 cases from our own records. Thirty cases, usually having been regarded as examples of this condition, were rejected from present consideration because of the brevity of the report or lack of history or physical examination. Six cases were discarded because of the possibility that the neoplasm may have been primary in the stomach in two cases, in the gallbladder and kidney in one each, while in one case the neoplasm was not definitely malignant, and in another, the tumor was probably a malignant melanoma. One hundred fifty-eight cases were rejected because of the lack of gross and microscopic studies of the primary lesion.

Appended are lists of the sources of the case reports of those cases judged acceptable for analysis (222), and those which were rejected for the reasons given (194).

CITATION OF THE SOURCE OF THE 222 CASES ANALYZED

Féréol; Rosenstein; Merkel, Cases 1 and 2; Caillet; Bridge; Fischel; Berry and Cockle; Barth and Marfan; Sacci and Adserson; Ely; Morax; Pilliet; Coats and Finlayson; Warmburg; May; Köster; Schmitt, Cases 1 and 2; Weir; Hesper, Case 1; Holtbuer, Case 2; Ely; Lannois and Courmont; Deetjen; Rendu; Hanot; Hanot; Thomas and Noica; Mauclaire and Durriex; Krokiewicz; Hughes; Descos and Bériel; Dominici; Dieckmann; Luzzatto; Dobbertin; Butz; Rolleston; Schüller, Cases 1 and 2; Mayo; Edes; Rixford; Maury; Scheuer; Miodowski, Cases 1 and 4; Hall; Hagen; Cornil and Chevassu; Moore; Klotz, Cases 1 and 2; Hultgren; Letulle and Verliac; Chardon and Raviart; Arnsperger, Cases 28 and 30; Raviart and Lorthois; Carnot and Harvier; Geiser, Case 2; Pappenheimer; Verhoogen; Souques and Aynaud, Cases

1 and 2; di Giovine; Le Blanc; Borelius, Case 4; Devic and Savy; Gasbarini; Rauzier; Rimbaud and Anglada; Le Noir and Courcoux; Körte, Case 32; Koerber, Cases 1 and 2; Oehler; Navarro; François-Dainville; Doberauer; Cuneo; Kausch, Cases 1, 2 and 4; Lenormont and Courmont; Cade; Oppenheimer; Upcott, Case 2; Roger and Lapeyre; Outerbridge; Binda; Pollet; Zuccola, Cases 1, 2, 3 and 4; Docq and Van Bever; Crohn, Cases 1, 2 and 3; Pétren, Case 56; Anschütz; Oliani, Case 9; Schüssler, Case 9; Ristori; McGuire and Cornish, Case 1; Pallin, Cases 1, 2 and 3; Carnot and Libert; Propping; Lewis; Brütt, Cases 6 and 7; Kleinschmidt, Cases 1 and 2; Tenani; Hartmann; Angeli; Pozzi, Cases 2 and 3; Prat, Case 1; Marino; Abell, Cases 2 and 3; Chiray, Benda and Milochevitch; Einhorn and Stetten; Pozzi, Cases 1 and 2; Konjetzny; Muller; Hadfield; Cabot, Case 12063; Garcia Lagos, Ugón and Dominiquez; Hingst, Cases 1, 2 and 3; Clar; Fulde; Rouslacroix, Raybaud and Debernardy; Cohen and Colp, Cases 1, 2, 4, 5 and 8; Murgoci, Case 1; Savinych, Cases 1 and 2; Del Valle, Brachetto-Brian and Orosco, Case 2; Busch; Dewis and Morse, Case 6; Boston and Jodzis; Jermain; Bonanno; Countryman; Meyer and Rosenberg, Case 1; Sisto; Varangot, Cases 1 and 14; Ross and Davie; Godfrey and Sappington; Mateer and Hartman, Cases 2, 3, 4 and 5; Rutishauser, Cases 2, 3 and 6; Walters; Pemberton; Judd; Block; Goldberg; Potter; Bérard, Mallet-Guy and Croizat; Lauwers, Cases 1 and 2; Cabot, Case 19191; Lisa; Levine and Fitz Hugh; Lami; Santero, Cases 1 and 2; Swenson and Levin; Chiuchini; Harbin, Harbin and Harbin; Whipple, Parsons and Mullins, Cases 1, 2 and 3; Hunt and Budd; Doub and Jones, Case 2; Koch, Case 2; Dardinski; Cabot, Case 23282; Geisthövel, Cases I–1, II–1 and II–8; Hoffman and Pack, Cases 3, 8, 11, 12, 15, 16 and 18; La Manna, Case 1 and Lieber, Stewart and Morgan, 17 cases.

CITATION OF THE SOURCE OF 30 CASES REJECTED BECAUSE OF INSUFFICIENT DATA

Oestreich; Leith, Cases 1 and 2; Lejonne and Milanoff; Krause; Geiser, Case 4; Saltykow, Cases 1 and 3; Schüssler, Case 3; Mariconda; Dalla Valle, Cases 1 and 2; Staemmler, Cases 1, 4 and 5; Mosto, Case 2; Plenge, Case 1; Llambias, Brachetto-Brian and Orosco, Case 3; Shapiro and Lifvendahl, Cases 4, 6, 8 and 11; Molfino; Schönbauer and Bsteh, Cases 1, 2, 3 and 4; La Manna, Case 153/31, and Nickerson and Williams, Cases A–35–11 and A–35–217.

CITATION OF THE SOURCE OF SIX CASES REJECTED BECAUSE OF PROBABILITY OF INCORRECT DIAGNOSIS

Reynolds; Krielke; Zuccola, Case 5; Hoffman and Pack, Case 4; Wahl and Zuccola, Case 7.

CITATION OF THE SOURCE OF 158 CASES REJECTED BECAUSE OF OMISSION OF PATHOLOGIC EXAMINATION

McNeal; Ehrmann; Stokes; Dittrich, Cases 1 and 2; Lacaze; Duchek; Lambl; Frerichs; Arrachard; Riesenfeld, Case 69; Avezou; Chouppe; Hicks; Martha; Mason; Courmont and Lannois; Fränkel; Holtbuer, Case 1; Terrier, Case 1; Thomas; Stabel; Morini; Auerbach, Cases 6 and 7; Kehr, Eilers and Lucké, Case 13; Pratt and Fulton; Halsted, Case 2; Pennato, Cases 1 and 2; Brill; Peaudeleu; Sears; Friedheim, Case 4; Czerny-Arnsperger; Arnsperger, Cases 27 and 29; Cordua; Geiser, Case 3; Boxwell; Aronson; Orth; Lennander; Köster; Chauffard; Bauer; Leclerc; Tartanson and Bonnamour; Stieda, Cases 10 and 13; Cade and Leriche; Morian, Cases 2 and 3; Ollive and Collet; Richards; Barjou and Gaté; Paus, Cases 210 and 211; Kausch, Case 3; Upcott, Case 1; Slajmer; Erdmann; Clermont; Zuccola, Case 6; Hirschel; Wrede; Erdmann and Heyd, Case 3; Pels-Leusden; Lichty, Cases 4 and 5; Schüssler, Cases 6, 7, 8 and 10; Oliani, Cases 1, 2, 3, 4, 5, 6, 7 and 8; McGuire and Cornish, Case 2; Di Poggio; Gandusio; Blad; Disque; Brütt, Cases 1, 2, 3, 4 and 5; Mucharinski; Pozzi, Case 1;

Dalla Valle, Cases 3, 4, 5, 6, 7, 8 and 9; Vedel, Giraud and Puech; Abell, Case 1; Staemmler, Cases 6, 7 and 8; Abramowa, Cases 1, 2 and 3; Eusterman, Berkman and Swan, Cases 7, 8, 9, 10, 11 and 12; Gohrbrandt; Joffe, Cases 1 and 2; Ceconi; Cohen and Colp, Cases 3, 6 and 7; Dewis and Morse, Case A; Cabot, Case 15241; Kulakov; Dencks, Cases 3 and 5; Klinkert; Blomström, Case 3; Colella; Ramlau-Hanson, Cases 5, 7, 8 and 9; Hinton, Case 2; Varangot, Case 2; Hartmann, Cases 11, 12 and 13; Walzel; Raiford, Cases G-1196, G-9310 and G-9923; Lee and Totten, Case 2; Startz; v. Hrabovsky, Case 1; Pángaro, Case 2; Hoffman and Pack, Case 17, and Geisthövel, Cases II–2, 3, 4, 5, 6, 7, 9, 10, 11 and 12.

The minutiae of the clinical phenomena evidenced and laboratory data obtained in each of the appended 17 case reports have, to a large extent, been omitted owing to the resultant unessential lengthening of the report; emphasis, however, has been made in detailing the postmortem findings and the results of the pathologic examinations.

CASE REPORTS

Case 1.—D. K., white, male, age 57, was admitted to the Uniontown Hospital, December 17, 1935, complaining of pain in the upper abdomen, jaundice, loss of 25 pounds in weight (11.3 Kg.) and vertigo. For the past 40 years the patient had suffered from digestive disturbances after eating certain foods. Such an episode occurred one month before admission to the hospital, followed one week later by jaundice which deepened progressively over a period of two weeks and then diminished somewhat. The appetite remained good, the bowels regular and the stools were clay-colored and foul. Shortly before admission, the patient experienced a dull, aching sensation in the lower abdomen and pain in the epigastrium accentuated by certain foods such as meats, fruits and nuts.

Physical Examination.—The abdomen was soft and no masses were palpable. There was, however, tenderness over the region of the gallbladder. Roentgenologic studies showed no evidence of gastric malignancy. Icterus index, 80; the bromsulfalein test for liver function showed 70 per cent retention of the dye in 30 minutes (2 mg. dosage); the van den Bergh test was immediate direct. *Clinical Diagnosis:* Carcinoma of the head of the pancreas. A cholecystogastrostomy was performed 11 days after admission. The convalescence was unsatisfactory, the jaundice increasing appreciably, and death occurred January 2, 1936.

Autopsy.—Three hours after death: Dr. H. Lund. The combined gross and microscopic diagnoses were: (1) Primary adenocarcinoma of the duodenal papilla; (2) obstruction of the common bile and pancreatic ducts; (3) surgical cholecystogastrostomy opening, with extensive hemorrhage into the gallbladder occluding the stoma; (4) jaundice; (5) acute degeneration of liver and kidneys; (6) moderate arteriosclerosis of aorta; (7) marked myocardial degeneration; (8) congestion and edema of lungs; (9) biliary stasis of liver; (10) chronic pancreatitis; (11) biliary nephrosis; (12) bilateral adenoma of adrenal glands; and (13) absence of right testicle.

There was slight edema of the extremities. The margins of the abdominal incision were well approximated superficially, but in and beneath the muscle layers there was a moderate amount of extravasated blood. Near the upper pole of the incision there was a small hematoma which communicated with the peritoneal cavity through a small gap in the serosa. The peritoneal cavity contained 600 cc. of red, watery fluid and there were large clots of blood about the gallbladder. The serosa was everywhere smooth and glistening.

All the cardiac chambers and valvular rings were dilated; the endocardium was stained yellow and the myocardium was soft. The lungs were voluminous, heavy, con-

gested and edematous in the dependent portions. The kidneys were deep green and the markings on the cut surface were indistinct.

The esophagus showed nothing noteworthy. The stomach was dilated to a capacity of 2,000 cc. and its wall was thin and attenuated. On the anterior superior aspect, 4 cm. proximal to the pylorus, there was an opening 1.5 cm. in diameter. This communicated with the cavity of the gallbladder which was distended with firm blood clots. Bile could not be forced through this cholecystogastrostomy opening.

Upon opening the duodenum, the papilla of Vater was located 7 cm. from the pyloric ring and appeared as a cylinder, 1.5 cm. long and 1.3 cm. in diameter, projecting outward and downward from the wall of the duodenum. It was moderately firm and its sides were apparently covered by duodenal mucous membrane. Its distal end was slightly rounded and presented a finely lobulated surface. On incising through the mass into the common bile duct, a moderate amount of mucoid fluid escaped. The ampulla of Vater felt slightly nodular, principally on its inferior and right surfaces,

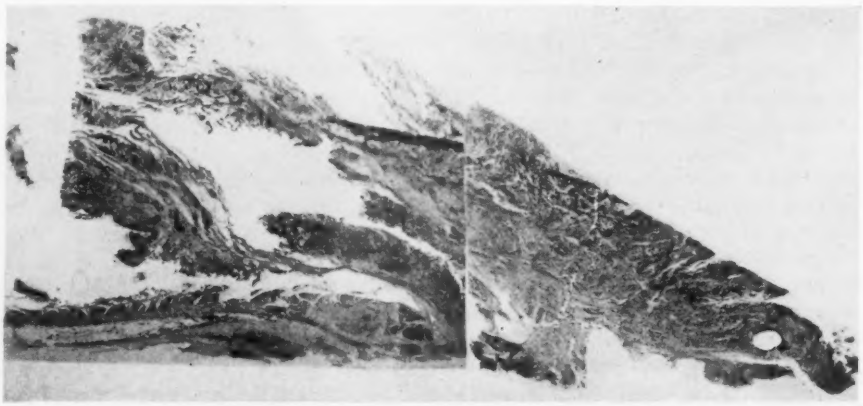


FIG. 1.—Case 1: A triangular section through the ampulla of Vater. The base is formed by portions of the muscular wall of the duodenum and pancreas. The hypotenuse is formed by the wall of the common bile duct. The upright side is formed, in its lower portion, by the reflected mucosa of the duodenum and the upper portion by the projecting papilla of Vater. (×7)

and the mucous membrane was light yellow and glistening. The wall of the ampulla was thickened by moderately firm, homogeneous light yellow tissue which was most abundant near the junction with the duodenum. Higher up, around the bile duct, this tissue faded into light gray streaks resembling fibrous tissue which was continuous with similar tissue in the pancreas. The common bile duct measured 2 cm. and the common hepatic duct 2.7 cm. in circumference.

The liver weighed 1,400 Gm. It was greenish-yellow, softer than normal, and the cut surface showed dilated biliary ducts.

The pancreas measured 18 cm. in length and was tough, with indistinct lobules. In the body of the organ the pancreatic duct measured 2.3 cm. in circumference and in the tail, 1.8 cm. It narrowed considerably toward its termination, coursing parallel with the common duct, and emptied into the duodenum through the ampulla of Vater just behind the orifice of the common duct. The pancreatic tissue was extensively atrophied, especially in the body of the organ, where it formed a grayish-yellow tough wall 6 mm. thick around the pancreatic duct. The head of the pancreas was very hard, cut with increased resistance and on section appeared to be mainly made up of tough grayish-yellow fibrous tissue containing a few small yellow areas which were taken to be pancreatic lobules. No enlarged lymph nodes were observed. The small intestines were moderately dilated and filled with gas and mucus.

*Pathologic Examination.**—A roughly triangular section of the ampulla of Vater was obtained for histologic examination, after the common duct was opened. A portion of the wall of the duodenum was attached to one corner of the section corresponding to the right angle (Fig. 1). The mucosa of the duodenum was reflected upward on the upright side while the muscular layer formed part of the base of the triangle. The greater portion of the upright side of the triangle (1.75 cm.) was formed by the projecting papilla of Vater; the hypotenuse (4 cm.) was formed by the wall of the common bile duct; the base (3.8 cm.) was composed of portions of the muscular wall of the duodenum, and pancreas. The papilla of Vater overhung the duodenum a little where the two structures met. A deep cleft traversed the section from the middle of the vertical side to the middle of the base, paralleling the hypotenuse or common duct. This structure will be referred to as "pancreatic duct." It was either the duct of Wirsung or a deep cleft between two very long villous-like projections. It appeared to terminate between the lobules of the pancreas. Its epithelium on the surface was autolyzed in places, but otherwise its structure was no different from the remainder of the atypical epithelium.

This "pancreatic duct" ended abruptly about 2 cm. from the tip of the ampulla, terminating in a pocket lined by flattened cells, surrounded by fibrous tissue and lying between atrophic pancreatic lobules. The strip of duodenal mucosa showed autolytic changes in the superficial epithelial cells but the outlines of the cryptic villi and Brunner's glands remained. Where the duodenal mucosa was reflected onto the papilla of Vater it narrowed abruptly and was capped by masses of atypical epithelial cells, and the underlying duodenal musculature faded out into the walls of the common duct and "pancreatic duct." These atypical epithelial cells lined both ducts and permeated extensively the deeper strands of fibrous and muscular tissue almost throughout the limits of the section, that is, about 3.5 cm. from the tip of the ampulla. Approximately 1 cm. of the distal end of the common duct was lined by nonmalignant partially autolyzed epithelium. The atypical epithelial cells measured approximately 10 micra in width and 50 micra in length and were characteristically arranged in a single layer, with the nuclei occupying the basal fourth of the cell. With this essential structure predominating, the epithelium was occasionally differently arranged to afford a small variety of appearances. On the surface there were numerous villous-like projections supporting numerous secondary papillary projections arranged in a parallel fashion, resembling duodenal crypts, although much wider. In the deeper tissues these large villi were less evident, and acinar structures predominated which were lined by single-layered epithelium either indented by papillary projections or traversed by fibrous septae.

The most common picture in the deeper tissue was that of large acini, almost completely filled with desquamated epithelium and imperfectly lined by single layers of epithelial cells. The individual cells were tall columnar with light pink, slightly foamy cytoplasm and sharply defined cell borders. The nuclei were generally ovoid or round and composed of a delicate stippling of chromatin material. Some cells had large hyperchromatic nuclei with coarse masses of chromatin. About one mitotic figure was observed in every two or three high power fields. The stroma was composed of fibroblasts, capillaries and inflammatory cells and formed broad bands on the surface supporting the villous-like projections. Several strands of smooth muscle were observed in the depth of the section and these were infiltrated by tumor cells However, the large strip of duodenal musculature and underlying pancreas did not seem to be invaded.

A section of pancreas was obtained from the head of the organ close to the common duct. The major part of the section was composed of mature, occasionally hyalinized fibrous tissue in which there were small ducts, atrophied lobules and islet tissue. The

* The pathologic examinations in all of the 17 cases reported herewith were made by Drs. Marshall M. Lieber and Harold L. Stewart.

intralobular and periductal fibrous tissue was increased and infiltrated with chronic inflammatory cells.

The inner half of the liver lobule was sharply demarcated owing to the anuclear, deeply pigmented and granular state of the hepatic cells. The pigment varied somewhat in amount in individual hepatic cells but in general was abundant, appearing as a fine stippling of large green granules, and bile thrombi were numerous in the canaliculi. In the peripheral zone the nuclei were generally well preserved and the cytoplasm contained relatively much less pigment. Some cells were multinucleated and the nuclei varied in size, some being hyperchromatic. The portal radicals were moderately thickened by fibrous tissue and infiltrated with small round cells and occasionally neutrophils.

The most striking change in the kidneys involved the convoluted tubules and consisted of extensive degeneration, necrosis and pigmentation. In the collecting tubules fewer of the cells were necrotic but many were swollen and granular and a few contained pigment. Bile pigment in the form of granules and casts was present in the lumens of the tubules. A few wedge-shaped or linear streaks of atrophic renal tissue were observed near the surface.

Case 2.—M. M., a white female, age 58, was admitted to the Philadelphia General Hospital, July 23, 1934. She had become acutely ill one month previously with nausea and epigastric pain but was unable to vomit. The pain was dull in character and localized under the right ribs. Jaundice appeared two weeks later and the urine became dark brown and the stools gray-colored.

Physical Examination of the abdomen was unsatisfactory owing to the marked obesity (220 pounds [100 Kg.]); it was, however, distended. Enlargement of the liver was present but no tenderness or palpable masses were noted. Roentgenographic examination of the gallbladder showed failure of the viscus to concentrate. The icterus index varied from 116 to 135 and the van den Bergh reaction was immediate positive. The patient gradually became weaker and died in coma, August 28, 1934.

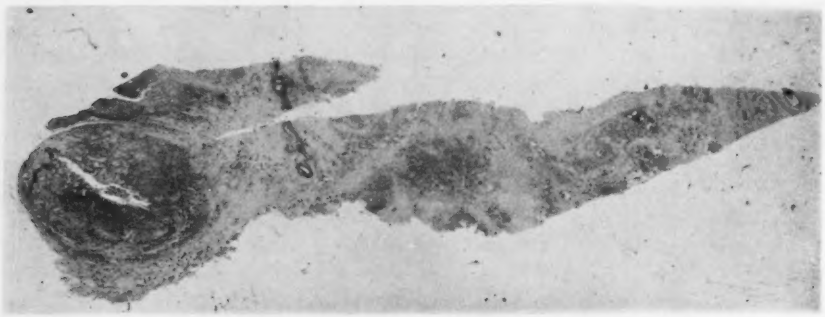
Autopsy.—Seven hours after death: Dr. R. A. Mathews. The combined gross and microscopic diagnoses were: (1) Adenocarcinoma, primary in the region of the papilla of Vater with extension to the pancreas and metastasis to the lung; (2) hydrohepatosis with marked jaundice and marked degeneration of the liver; (3) obstruction of pancreatic ducts, chronic pancreatitis and foci of fat necrosis; (4) bile pigmentation of kidney and marked nephrosis; (5) arteriosclerosis of aorta and coronary arteries; (6) myocardial degeneration and sclerosis of mitral and aortic valves; (7) generalized passive congestion; and (8) bronchopneumonia.

The gastro-intestinal mucosa appeared congested and the contents of the colon were clay-colored. At the papilla of Vater there was a small, dense, firm, yellow nodule 1 cm. in diameter. By compressing the gallbladder with considerable force, bile could be forced through the opening of the papilla into the duodenum. Proximal to the obstruction the biliary passages were markedly dilated. The gallbladder was distended downward 4 cm. below the costal margin; its wall was thick, the mucous membrane smooth and bile-stained and it contained thick black-brown bile. The liver weighed 2,020 Gm.; its capsule was smooth and the parenchyma was yellowish-brown and friable with small, indistinct lobular markings. The pancreas was enlarged and the cut surface showed patches of yellow necrotic material and a pitted, honey-combed appearance due to dilated ducts.

Pathologic Examination.—A section was taken through the duodenum including all coats and a small amount of fat and connective tissue externally. No evidence of the papilla, bile ducts or pancreatic duct was observed in this section. The mucous membrane and underlying glands of Brunner appeared intact. Tumor tissue was observed in the submucous and muscular coats and the fibro-fatty tissue outside the duodenum. Tumor cells were observed in and around blood vessels and nerves. The atypical cells grew in the form of small irregular acini and clumps. They were chiefly

columnar or cuboidal and were relatively small with smooth, pale or bright red cytoplasm and small oval nuclei which were exceedingly hyperchromatic although regular in shape. A few of the tumor cells were large, irregular and multinucleated; mitotic figures were rare. The stroma was abundant and consisted of dense, hyalinized fibrous tissue, comparatively avascular and containing only a few inflammatory cells. Large areas were completely necrotic and in these there were small hemorrhages.

FIG. 2.



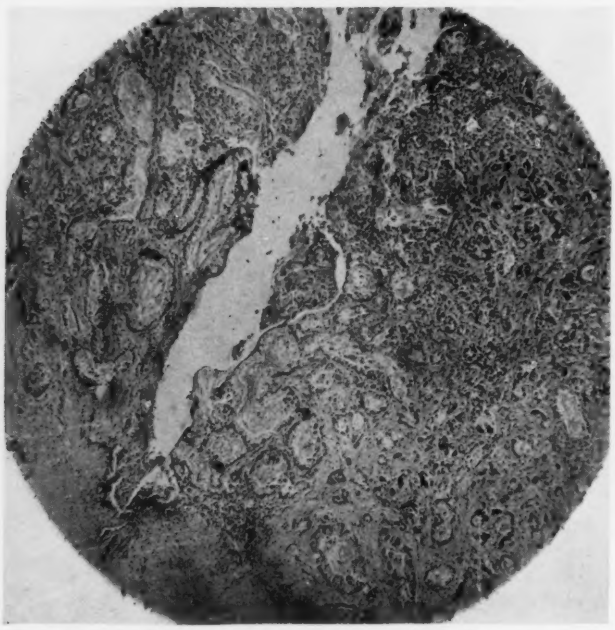


FIG. 3.

FIGS. 2 and 3.—Case 2: Two views of a large duct embedded in pancreatic tissue. The lumen of the duct is slit-like and there are several shallow areas of ulceration on the surface. The mucous membrane is permeated with densely packed neoplastic tissue. (×10 and ×40, respectively)

Another section passed through a large duct, 0.4 cm. in diameter and with a narrow slit-like lumen embedded in pancreatic tissue (Fig. 2). The mucous surface of this duct, its entire wall and the surrounding tissue were composed of densely packed neoplastic tissue resembling that just described (Fig. 3) and there were several shallow areas of ulceration on the surface.

Sections of the pancreas showed dilatation of ducts, atrophy, fatty infiltration, extensive fibrosis, large areas of necrosis involving pancreatic and fat tissue with associated inflammatory cell reaction including lymphocytes, polymorphonuclear leukocytes and mononuclear cells. The islands of Langerhans tended to persist in the areas of atrophy and fibrosis.

The myocardium showed fibrosis, fatty infiltration and acute degeneration. A section of lung contained a single small metastatic nodule. There were areas of bronchopneumonia and thrombosis of the pulmonary vessels. The adrenal gland contained many focal collections of lymphocytes, especially in relation to the veins. The kidney showed a moderate grade of biliary pigmentation, and marked degeneration and necrosis of tubular epithelium. There were widespread necrosis and disintegration of the liver tissue, less than 5 per cent of the hepatic cells appearing viable. Many of the hepatic cells were vacuolated and there was marked biliary pigmentation. The portal areas were thick and fibrous, and contained many lymphocytes and small proliferating bile ducts.

Case 3.—T. I., white, male, age 48, was admitted to the Philadelphia General Hospital, February 1, 1934, complaining of epigastric pain and exhibiting deep jaundice. He had had painful attacks accompanied by jaundice in 1929, and again in 1932. *Clinical Diagnosis:* Acute cholecystitis. Cholecystectomy was performed, August 29, 1932, at another hospital. With persistence of the symptoms, the patient was again operated upon December 19, 1932, a duodenostomy and removal of a fistulous tract being performed. The terminal illness developed January 20, 1934, characterized by a steadily deepening jaundice and clay-colored stools followed ten days later by sudden sharp pain in the right upper quadrant of the abdomen. There had been no nausea or vomiting at any time.

Physical Examination demonstrated a rounded abdomen, somewhat distended and extremely tender and rigid over the epigastric area; there were no masses, however, and the liver was not palpable. Roentgenographic studies of the gastro-intestinal tract showed the stomach in the midabdomen, hypotonic and slightly ptosed with the greater curvature below the iliac crest. Peristaltic movements were inactive and passed uninterruptedly along both curvatures. The duodenal cap was visualized and seemed normal. About 20 per cent of the barium was retained at the end of six hours. *Roentgenologic Diagnosis:* Duodenal adhesions and enlargement of the liver and spleen. The icterus index was 52 and the van den Bergh reaction was immediate direct with 70 mg. of bilirubin per 100 cc. of blood.

During the patient's stay in the hospital, the jaundice deepened, abdominal distention increased and the liver became palpable two fingers' breadth below the costal margin. He developed hiccoughs and paralytic ileus a few days before death, which occurred on February 10, 1934. The clinical diagnoses were obstructive jaundice, stone in the common bile duct, cholangeitis and hepatitis.

Autopsy.—Twelve hours after death: Dr. L. L. Lanyon. The gross anatomic findings were: (1) Malignant duodenal ulcer surrounding the papilla of Vater; (2) marked dilatation of the common bile duct; (3) chronic cholecystitis; (4) calculous obstruction of the intrahepatic biliary radicles; (5) multiple liver abscesses confined mainly to the left lobe; (6) congestion and degeneration of the pancreas; (7) myocardial degeneration with passive congestion; and (8) cholemic nephrosis.

Pathologic Examination.—The section of duodenum was lined by partially autolyzed mucous membrane, in the depths of which a malignant transformation was in progress. The atypical epithelial cells extended through the submucosa and muscular coats and were observed invading nerve fibers. The neoplastic cells varied considerably, with deeply acidophilic cytoplasm and hyperchromatic nuclei of varying size and shape, which were occasionally observed in mitosis. The cellular arrangement was in the form of nests, short cords and acini, the latter being frequently lined by tall

columnar cells with dark blue, basally situated nuclei. The connective tissue stroma was rather scanty and contained collections of lymphocytes.

A single section through the pancreas and common bile duct disclosed invasion of both these structures by tumor tissue. In other sections from the pancreas there was a moderate amount of fibrosis and inflammatory cell reaction about the ducts and within the lobules.

The liver tissue showed few of the features of biliary stasis, with little or no bile pigment present. In the inner portions of the lobules there was considerable sinusoidal congestion and degeneration and atrophy of the parenchyma. The hepatic cells showed active signs of regeneration with multiple nuclei and hyperchromasia. Peripherally there was a marked amount of fibrosis in and about the lobules and small abscesses were frequently observed.

Case 4.—F. T., colored, male, age 50, was admitted to the Philadelphia General Hospital February 10, 1933, complaining of stomatitis, marked jaundice and loss of weight. Over a period of years the patient had had digestive disturbances and for the last 18 months had noticed dyspnea on exertion. The terminal illness was initiated, seven weeks before admission to the hospital, by salivation and intense itching followed a week later by dark urine, clay-colored stools and jaundice and later by stomatitis and considerable loss of weight. There had been no constipation or unusual digestive disturbances at this time.

Physical Examination showed the spleen and liver to be both enlarged and pain was elicited on deep pressure over the liver. Roentgenographic studies disclosed a dense shadow in the region of the gallbladder; the stomach appeared hypertonic and the duodenal cap irregular. Icterus index 165; van den Bergh reaction immediate positive with 17.6 mg. of bilirubin per 100 cc. of blood. *Clinical Diagnosis:* Metallic poisoning. The patient became gradually weaker and died February 27, 1933, with the clinical signs of localized peritonitis.

Autopsy.—Thirteen hours after death: Dr. H. McCutcheon. The combined gross and microscopic diagnoses were: (1) Peripapillary adenocarcinoma of duodenum; (2) hydrohepatosis with marked jaundice; (3) obstruction of pancreatic ducts with marked fibrosis; (4) biliary pigmentation of kidneys and mild nephrosis; and (5) suppurative bronchopneumonia.

Upon opening the duodenum a retracted scar, presumably a healed ulcer, was observed on the mucous surface of the pyloric ring. The papilla of Vater was surrounded by a nodular, pale growth measuring 2 cm. in diameter, which obstructed the common bile duct. Proximal to the lesion the biliary passages were enormously distended and clear, dark-yellow bile could be forced through the papilla by making pressure on the gallbladder. The liver weighed 1,730 Gm. and was dark green with accentuated liver markings.

Pathologic Examination.—The section of duodenum consisted on either side of a strip of partially autolyzed mucous membrane with a few Brunner's glands in the submucosa. In the center of the section there was a shallow depression, the base and margins of which exhibited a carcinomatous change, and beyond this was a large tumor nodule (Fig. 4). Upon approaching this lesion the epithelial cells of the mucous membrane became hyperchromatic and atypical in the deeper portions of the crypts. The glands became elongated and broke through the submucosa, spreading out laterally and deeply infiltrating all coats of the duodenum (Fig. 5). As a rule the tumor cells were tall columnar, fairly regular and arranged in elongated acini with a lining one to several layers thick. The nuclei occupied a basal situation in these cells and there were approximately one or two mitotic figures per high power field. There were a few other acini which were small, round or imperfectly formed and lined by polyhedral or flattened cells which were frequently necrotic and desquamated. There was little tendency for the cells to grow in the form of clumps or nests. The supporting stroma was of adult connective tissue, relatively avascular, rather scanty in amount and infiltrated

with small round cells. Chronic inflammatory changes were observed in the subserosa over a considerable distance.

FIG. 4.—Case 4: A section of duodenum showing hyperplastic changes in the mucous membrane and terminating in a large neoplastic nodule to the left. (×10)

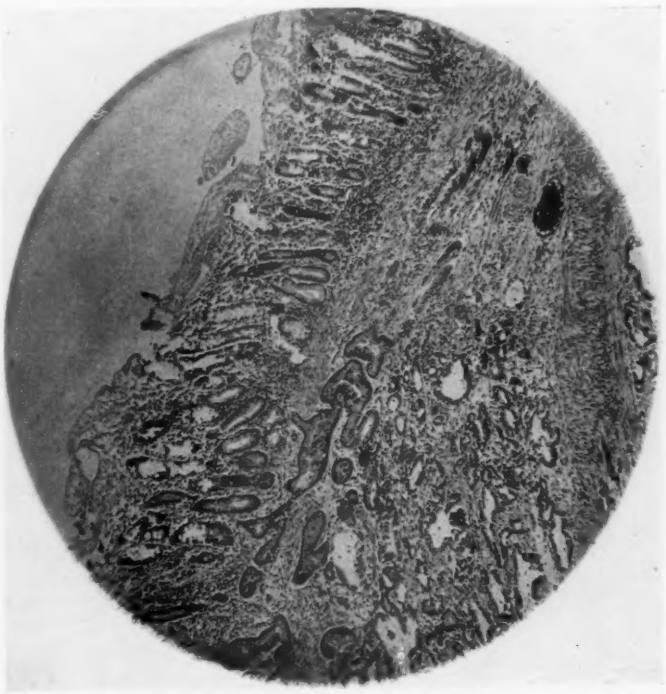


FIG. 5.—Case 4: Duodenum showing point of malignant transformation. The glands are elongated and have broken through the submucosa to infiltrate deeply all coats of the bowel. (×40)

The characteristic features of biliary stasis were observed in the liver with pigmentation and degeneration about the central and sublobular veins and focal midzonal and biliary necroses. The portal radicles were moderately thickened by an eosinophilic and

round cell infiltration and proliferation of fibrous tissue and small biliary ducts. The variation in the appearance of the nuclei in the inner portion of the lobule suggested a rather marked degree of hepatic cell regeneration but no mitotic figures were observed. There was marked biliary pigmentation of the renal tissue and a mild grade of nephrosis.

The head of the pancreas was infiltrated with lymphocytes, mononuclear cells and connective tissue mainly peri-acinar, perilobular and periductal in distribution. There was an associated atrophy and distortion of the acini and some proliferation of the ductal epithelium. A few ducts were dilated, lined with flattened epithelial cells and filled with a finely fibrillar, faintly eosinophilic material.

Case 5.—F. C., white, female, age 82, was admitted to the Philadelphia General Hospital September 18, 1931, suffering from abdominal pain, jaundice, anorexia, emaciation and dehydration. The onset had occurred three weeks previously with severe, intermittent pain in the right upper abdominal quadrant. This was soon followed by deep jaundice.

Physical Examination demonstrated tenderness in the right upper abdominal quadrant and the liver was palpable four fingersbreadth below the costal border. Icterus index was 280; the van den Bergh reaction was immediate direct and there were 24 mg. of bilirubin per 100 cc. of blood. Death occurred October 1, 1931.

Autopsy.—Five hours after death: Dr. H. L. Stewart. The combined gross and microscopic diagnoses were: (1) Peripapillary carcinoma of the duodenum with extension to the pancreas and surrounding adhesions and with metastases to the liver and a regional lymph node; (2) hydrohepatosis with marked cirrhosis and jaundice; (3) calculous cholecystitis with obliteration of the cystic duct; (4) obstruction of duct of Wirsung; (5) biliary pigmentation of the kidney with marked nephrosis; and (6) acute degeneration of the myocardium.

The stomach, duodenum, pancreas, liver and gallbladder were tightly bound together by dense adhesions. Upon opening the duodenum, the papilla of Vater was found to be surrounded and obstructed by a large, firm fungating mass composed of smaller nodules which were yellow and white when incised. This tissue extended through the wall of the duodenum to infiltrate the pancreas and surrounding adhesions. The duct of Wirsung measured 1.5 cm. in diameter. The common bile duct measured 7 cm. in circumference and contained thin yellow, mucus-like fluid. The nodular lesions surrounding the papilla of Vater extended for a distance of 4 cm. into the common bile duct. The cystic duct was obliterated. The gallbladder was markedly thickened and tightly contracted around two large, nonfaceted, finely granular calculi; it contained no bile. The liver was nodular and mottled yellow and black. It cut with increased resistance exposing a surface composed of small nodules which had replaced the normal structure of the organ. In addition there were several nodular lesions throughout the liver which measured approximately 2 cm. in diameter and presented the same appearance as the tissue about the papilla of Vater. Similar areas were observed in a lymph node at the junction of the common and cystic ducts.

Pathologic Examination.—The section passed through the terminal portion of the common bile duct and a piece of underlying pancreas. The mucosa of the common bile duct was thickened and thrown into plump papillary projections composed of anaplastic epithelial cells which penetrated through the wall of the common bile duct into the pancreatic tissue. These cells were round or polyhedral, with pale, fairly smooth cytoplasm and large irregular hyperchromatic nuclei, such as are occasionally observed in mitosis. They grew in the form of strands, cords, clumps and small irregular acini and, in large areas, were totally necrotic. Perivascular and perineural infiltration was noted. The connective tissue stroma was relatively abundant, comparatively avascular, occasionally hemorrhagic, and infiltrated with small round cells. In some areas the tumor cells bore a striking resemblance to the squamous cell type but definite pearl formation and prickle cells were not observed.

The pancreatic tissue was extensively infiltrated with tumor cells. It also showed perilobular and peri-acinar fibrosis, dilatation of ducts and, in large areas, necrosis.

The kidney showed nephrosclerotic changes with a moderate grade of nephrosis and slight biliary pigmentation.

Case 6.—K. M., white, female, obese, age 62, was admitted to the Philadelphia General Hospital August 28, 1932, complaining of weakness, loss of 40 lbs. (18.1 Kg.) over a period of six months and, latterly, nausea, vomiting and jaundice. There had been two episodes of painless jaundice lasting a week or ten days, one and three years previously. Jaundice had appeared three weeks before admission to the hospital and as it increased in intensity over a period of a week, there had developed pain, nausea, vomiting, fever, chills and clay-colored stools. The patient experienced several transitory painful seizures of a shooting character in the region of the gallbladder.

Physical Examination showed a very obese, elderly female with a definitely distended abdomen; there was no tenderness, rigidity or palpable masses; the liver and gallbladder were not palpable. The icterus index was 225; the van den Bergh reaction was immediate direct and there were 22.4 mg. of bilirubin per 100 cc. of blood. *Clinical Diagnosis:* Cholelithiasis; stone in the common duct. Vomiting continued; jaundice deepened progressively and death occurred, September 6, 1932.

Autopsy.—Four hours after death: Dr. H. L. Stewart. The combined gross and microscopic diagnoses were: (1) Peripapillary carcinoma of the duodenum with extension into the pancreas and metastasis to liver; (2) hydrohepatosis with marked jaundice; (3) obstruction of the duct of Wirsung; (4) calculous cholecystitis; (5) congestion and edema of lungs; and (6) acute myocardial degeneration.

The papilla of Vater was surrounded by a firm nodular papillary lesion which extended through the entire wall of the duodenum to invade the head of the pancreas for a short distance. The pancreatic and common bile ducts, although readily admitting the passage of a probe, were both obstructed; proximal to the papilla the bile ducts were enormously distended. The liver weighed 2,180 Gm. and presented a deep green mottling. Two small firm, button-like nodules 2 cm. in diameter were present in the capsule. The intrahepatic biliary ducts were distended with bile-stained purulent fluid. The gallbladder was tightly contracted about a single soft calculus which measured 2 cm. in diameter.

Pathologic Examination.—The section of duodenum presented an unbroken autolyzed mucous membrane, and scattered through all its layers were groups of atypical cells in acinar formation supported by a moderate amount of stroma. The majority of the tumor cells were well differentiated into tall columnar elements with basally situated hyperchromatic nuclei which were observed in mitosis, approximately once per high power field. Deeply, the tumor cells infiltrated a piece of attached pancreas for a short distance with, here and there, marked fibrosis and low grade inflammatory cell reaction with lymphocytes and mononuclear cells.

The hepatic tissue showed the features of early biliary stasis with pigmentation and degeneration in the inner portion of the lobules, focal midzonal areas of necrosis and early periportal fibrosis. Metastases were not observed in the sections of liver available for study.

The renal tissue was pigmented with bile and the tubular cells were degenerated.

Case 7.—W. J., white, male, age 60, was admitted to the Philadelphia General Hospital, May 25, 1932, with profound jaundice and loss of 55 pounds (25 Kg.) in weight. The illness began abruptly ten weeks previously with moderately severe, continuous epigastric pain which lasted for three weeks, at the end of which time it ceased completely; coincident with this there developed progressively deepening jaundice. The urine became dark and the stools clay-colored, but there was no nausea, vomiting or recurrence of abdominal pain.

Physical Examination did not demonstrate any palpable masses, tenderness or enlargement of the liver; there was, however, some fulness in the epigastrium. Roentgenographic

studies of the gastro-intestinal tract showed widening and stasis of the duodenal loop. There were 12 mg. of bilirubin per 100 cc. of blood and the van den Bergh reaction was immediate direct; the icterus index was 150.

A cholecystoduodenostomy was performed, June 28, 1932. The head of the pancreas was found to be enlarged and firm. The clinical manifestations of jaundice failed to abate following operation. The patient became gradually weaker and died, July 7, 1932.

Autopsy.—Eighteen hours after death; Dr. W. Brody. The combined gross anatomic and microscopic diagnoses were: (1) Peripapillary carcinoma of the duodenum with metastases to the lymph nodes; (2) hydrohepatosis with marked jaundice; (3) obstruction of the duct of Wirsung and chronic pancreatitis; (4) hemorrhage into the lumen of the gallbladder and peritoneal cavity; (5) bile pigmentation and acute degeneration of the kidney; and (6) myocardial degeneration.

The body tissues were deeply jaundiced. There was moderate dilatation of the stomach and the peritoneal cavity contained 1,200 cc. of bloody fluid which was believed to have originated from the operative wound in the neighborhood of the gallbladder. The papilla of Vater was surrounded and obstructed by a fungating ulcerated indurated lesion proximal to which the biliary passages were markedly distended, the common bile duct measuring 4 cm. in circumference. The lumen of the gallbladder was completely occluded with clotted blood which effectually obstructed the flow of bile from the cystic duct into the duodenum through the cholecystoduodenostomy opening. The liver weighed 1,700 Gm.; its cut surface was mottled deep green and studded with bile ducts filled with green bile. The duct of Wirsung admitted the passage of an ordinary pencil. The head of the pancreas was extremely firm and the tail contained numerous cysts; on section, the pancreatic tissue was lobulated and contained homogeneous areas throughout the gland, suggestive of neoplastic invasion. There was no mention of the lymph nodes in the protocol.

Pathologic Examination.—The duodenum could not be positively identified in any of the sections available for study. In one section of autolyzed fibromuscular tissue (probably duodenum) and in several others containing lymph nodes. there were actively invasive, atypical epithelial cells arranged in elongated acini and small, solid clumps. The cells were moderately anaplastic in some areas while in others they preserved many of the characteristics of intestinal mucous membrane, being arranged in single-layered rows of tall columnar cells with basally situated nuclei. In some of the elongated acini, the epithelial cells were heaped up, forming short spur-like projections supported by a delicate stroma. The nuclei were irregular in places and hyperchromatic, with approximately two mitotic figures per high power field. A few small hemorrhages and several large areas of necrosis were observed.

The pancreas showed a marked increase in fibrous tissue, and lymphocytes in and around the lobules of the parenchyma, which was extensively atrophied.

The sections of liver presented the picture of marked biliary stasis. There was a marked grade of perilobular and intralobular fibrosis and proliferation of the smaller bile ducts.

There was biliary pigmentation of the kidney, marked nephrosis and thickening of the arterial branches.

Case 8.—J. B., white, male, age 74, was admitted to the Philadelphia General Hospital, July 7, 1931, suffering with abdominal pain, loss of appetite and deep jaundice. For years, the patient had had chronic, fibrous pulmonary tuberculosis with cavitation of both apices. His terminal illness began with loss of appetite, six months before admission to the hospital. During the next four months, he developed belching, vomiting after meals, and dull, constant abdominal pain. Icterus was first noticed six weeks before admission and gradually increased in intensity.

Physical Examination demonstrated some fulness and rigidity of the right hypochondrium but there were no definite masses and the liver was not palpable. Roentgenographic examination of the gastro-intestinal tract demonstrated hypoperistalsis and reten-

tion in the pyloric end of the stomach and first two portions of the duodenum. In the prone position there was a slight prepyloric irregularity. The conus and third portions of the duodenum were slightly dilated, and the first and second portions were displaced somewhat to the right and downward in a circular fashion. The patient grew progressively weaker and died, July 10, 1931.

Autopsy.—Fifty-two hours after death: Dr. J. F. Cohen. The combined gross and microscopic diagnoses were: (1) Peripapillary carcinoma of the duodenum with lymph node metastases; (2) hydrohepatosis with marked jaundice; (3) calculous cholecystitis; (4) chronic fibrous pulmonary tuberculosis with cavitation; (5) myocardial degeneration and fibrosis; (6) degeneration and biliary pigmentation of the kidney with calcification of tubular epithelium; and (7) acute fibrinous peritonitis.

The peritoneal cavity contained 200 cc. of brown, turbid fluid; the coils of intestine were adherent to each other and covered with bile-tinged, plastic exudate. The papilla of Vater was surrounded on all sides by a circular, ulcerative necrotic process, the margins of which were soft, round and elevated, while the base was firm and resistant to the touch. The infrapapillary portion of the duodenum was dilated; the stomach appeared normal. Proximal to the papilla, the common bile duct and hepatic ducts were dilated but the cystic duct was not involved in this process; the gallbladder was small, thick and fibrous and bound by adhesions to the colon and duodenum. The gallbladder was filled by a single, hard, cylindrical calculus, and in one area its mucous membrane was ulcerated. The liver appeared small; its surface was lobulated, mottled yellow and green, firmer than usual and apparently fibrotic. The pancreas was somewhat autolyzed. The lymph nodes appeared normal.

Pathologic Examination.—The section of duodenum consisted of hyperplastic mucosa changing at one place into disorderly columnar cells arranged in acini which penetrated deeply into the submucosa. This section of duodenum showed advanced autolytic processes so that the following description of the neoplasm is based upon the findings in one of the lymph nodes. This node was largely replaced by groups of tall columnar epithelial cells arranged in elliptical acini, most of which were large and resembled somewhat the crypts of intestinal mucosa. The cells were usually arranged in a single layer but in places, mounds of four to 12 layers were observed. The characteristic cell had acidophilic cytoplasm and round to ovoid nuclei usually situated at the basal pole. The nuclei were moderately hyperchromatic, and two to three mitotic figures per high power field could be found in different parts of the section. The atypical epithelial cells invaded the capsule of the node and spread out into the surrounding fibrous tissue.

Sections of the liver showed bile casts and pigmentation, degeneration and necrosis of the hepatic cells in the inner portion of the lobule. In the portal radicles, there was an increase in fibrous tissue, an infiltration of lymphocytes and a moderate degree of proliferation of the bile ducts.

Sections of the kidney showed a moderate degree of nephrosis and pigmentation, and numerous small discrete and confluent masses of calcium were observed. The position of many of these calcific deposits could not be positively identified, but others definitely appeared to lie within tubules, some of which were completely calcified. Several of the larger arteries were thickened and sclerotic.

Sections of pancreas were not available for study.

Case 9.—G. F., white, male, age 81, was admitted to the Philadelphia General Hospital, December 2, 1930, suffering from marked jaundice and intermittent chills and fever. The onset had occurred seven months previously, with chills and fever of the Charcot type and progressive, painless jaundice.

Physical Examination showed the abdomen to be protuberant, tense, and gave the physical signs of containing fluid. After removing 3,200 cc. of clear, bile-stained fluid, the liver edge was palpable four fingers' breadth below the costal border. Roentgenographic studies of the gastro-intestinal tract were unsatisfactory because of the patient's

inability to ingest sufficient barium. *Clinical Diagnosis:* Carcinoma of the head of the pancreas. The patient became gradually weaker and died, December 20, 1930.

Autopsy.—Two hours after death: Dr. H. Gunn. The combined gross and microscopic diagnoses were: (1) Peripapillary adenocarcinoma of duodenum; (2) hydrohepatosis with atrophy and fibrosis of gallbladder, cirrhosis of liver and marked jaundice; (3) obstruction of the duct of Wirsung with pancreatic fibrosis and fatty infiltration; (4) arterionephrosclerosis with parenchymatous degeneration and biliary pigmentation; and (5) myocardial fibrosis.

All the tissues were jaundiced and there were 1,500 cc. of straw-colored fluid in the peritoneal cavity. About 3 cm. above the papilla of Vater, a small nodule was found in the wall of the duodenum which, on section, proved to be cystic and contained milky fluid (minor papilla?). The papilla of Vater was surrounded by a cauliflower-like growth 3 cm. in diameter composed of firm papillary masses, finely granular in texture. The pancreatic duct opened into this mass and was dilated throughout its entire length. The glandular tissue of the pancreas was atrophic and largely replaced by fat. The bile ducts proximal to the papilla were greatly distended but the gallbladder was shrunken and atrophied. The liver weighed 1,560 Gm.; it was green and coarsely nodular and on section, the bile ducts were found to be dilated and filled with coarse débris.

Pathologic Examination.—The section of the duodenum contained a small area in which the mucous glands became somewhat atypical with hyperchromasia and irregularity of the epithelial cells; these penetrated into the submucosa and muscularis for a short distance. Another section of duodenum was covered with a narrow strip of hyperplastic mucous membrane which merged into an area of well differentiated papillary adenocarcinoma. The acini of the tumor were composed of oval, elongated crypts resembling closely the normal mucous membrane and they extended through all coats of the intestinal wall. The atypical cells were usually piled up in several layers on the walls of the acini and consisted of tall columnar elements with basally situated nuclei varying somewhat in size and shape but staining fairly uniformly. From two to six mitotic figures were observed per high power field. The stroma was not abundant; it contained numerous congested blood vessels, many of which were poorly developed, and was infiltrated with many lymphocytes.

The hepatic cells were intensely pigmented, moderately degenerated, loosened from the reticulum about several of the bile ducts and exhibited some evidences of regeneration in the inner portion of the lobule. There was a moderate degree of small bile duct proliferation and the portal areas were markedly thickened by fibrous tissue which extended into the periphery of the lobules, isolating hepatic cells singly and in small groups.

In a section of pancreas from the region of the common bile duct, the interstitial tissue was distributed abundantly about the lobules and acini and the associated parenchymal cells were markedly atrophied.

There was a moderate grade of nephrosclerosis with acute congestion and several small retention cysts. The tubular epithelium was slightly pigmented and showed rather marked degeneration and necrosis.

There was considerable interstitial fibrosis of the myocardium.

Case 10.—L. E., colored, male, age 56, was admitted to the Philadelphia General Hospital, August 27, 1930, in a semiconscious state, and no history was obtainable.

Physical Examination showed a well rounded mass, continuous with the liver, in the right upper abdominal quadrant and extending 6.5 cm. below the costal border. There was no abdominal rigidity, tenderness or evidences of fluid. *Clinical Diagnosis:* Chronic nephritis; chronic myocarditis and uremia. Two days after admission, the patient lapsed into coma and died.

Autopsy.—Four hours after death: Dr. W. H. Black. The combined gross and microscopic diagnoses were: (1) Peripapillary carcinoma of the duodenum with metastasis to a regional lymph node; (2) hydrohepatosis with marked jaundice; (3)

obstruction of the duct of Wirsung and chronic pancreatitis; (4) arteriosclerosis of the aorta and coronary arteries; and (5) severe biliary nephrosis.

The papilla of Vater was surrounded by a ring of indurated tissue which on section was white, opaque and appeared neoplastic. By exerting pressure on the gallbladder, bile could be forced through the orifice of the papilla which admitted a probe with difficulty. Proximal to the obstruction the biliary passages were markedly distended; the common bile duct measured 5.5 cm. in circumference, the hepatic duct 4.5 cm. and the cystic duct 3 cm. The gallbladder extended to the level of the umbilicus, its wall was thin and its lumen was distended with pale-green bile and "biliary mud." The liver measured 34x23x7 cm. and extended a hand's breadth below the costal margin. It was deeply bile-stained with prominent lobular markings and a thickened capsule over the gallbladder fossa.

The pancreas was indurated. The duct of Wirsung was dilated to a circumference of 3 cm. The duct of Santorini opened 2 cm. above the papilla of Vater. The stomach contained a considerable quantity of blood and its mucous membrane was thrown into prominent rugae dotted with petechial hemorrhages.

The kidneys were enlarged, weighing respectively 380 and 360 Gm. They were swollen, soft, grass-green in color and regular in outline. The capsules were adherent in a few places; the cut surface was mottled red and green with small greenish-black, punctate areas in the cortex.

The lymph nodes were large, soft and greenish-black.

Pathologic Examination.—The section of duodenum consisted of smooth muscle overlaid with submucosa containing Brunner's glands and above these a small remnant of partially autolyzed mucous membrane. Deeply, the mucosa merged into an area of immature epithelial cells which penetrated through the submucosa into the muscularis. These atypical epithelial cells were small, polyhedral and columnar in shape and tended to be arranged in acini, short rows and small nests of from one to several dozen cells embedded in dense connective tissue. The cytoplasm was acidophilic and the nuclei were hyperchromatic, basally situated in the columnar cells but occupied no characteristic position in the other cells.

The liver presented the picture of biliary stasis with associated pigmentary and regressive changes around the central and sublobular veins. No biliary or focal midzonal areas of necrosis were observed. There was a marked increase of connective tissue, predominately periportal but in some places diffuse and was most marked about the bile ducts. There was very little proliferation of the smaller bile ducts.

Sections of the pancreas showed marked perilobular and diffuse, hyalinized fibrosis with marked atrophy of the parenchyma.

The kidney sections showed marked bile pigmentation.

A section of a lymph node showed a metastatic tumor nodule with the characteristics of the primary lesion.

Case 11.—W. R., colored, male, age 65, was admitted to the Philadelphia General Hospital, July 9, 1928, suffering from jaundice, obstipation and incessant vomiting, which had begun two weeks previously. The patient was markedly dehydrated, weak and emaciated.

Physical Examination demonstrated epigastric resistance; there were no masses palpable. Icterus index 12. The van den Bergh reaction was delayed. *Clinical Diagnosis:* Intestinal obstruction either from intussusception or volvulus.

Autopsy.—Eight hours after death: Dr. D. R. Morgan. The combined gross anatomic and microscopic diagnoses were: (1) Peripapillary adenocarcinoma of the duodenum with metastasis to the liver; (2) hydrohepatosis with jaundice; (3) chronic pancreatitis; (4) cardiac hypertrophy with myocardial degeneration and fibrosis; and (5) congestion and edema of lungs.

The papilla of Vater was much thickened, firm and constricted, although bile could be forced through it into the duodenum by exerting pressure upon the gallbladder.

Proximal to the papilla, the extrahepatic biliary passages were all greatly dilated, the gallbladder being somewhat thickened, hyperemic and distended with dark, thick bile.

The liver, weighing 1,600 Gm., was dark and mottled in appearance and contained three slightly elevated pea-sized nodules on the surface. The lymph nodes along the course of the bile ducts were enlarged and firm. The pancreas appeared firm and fibrotic.

Pathologic Examination.—Two sections of the duodenum were available for microscopic study: in one of these, there was an extensive carcinomatous infiltration of the submucosa but the mucous membrane and Brunner's glands were uninvolved. In the other, there was extensive ulceration of the mucous membrane and beneath this, neoplastic cells permeated the nodules of Brunner's glands. It was not possible to determine whether or not the carcinomatous cells arose from intestinal epithelium. The neoplasm extended into the muscular coat in long strands, circular nests and elongated and branching cords supported by a scanty stroma supplied with well formed vessels. The cells grew, principally, in the form of solid masses but an imperfect attempt to reproduce glandular structure was common and occasionally acini were observed, with a single layer of tall columnar epithelium with basally situated nuclei suggesting an intestinal origin. In the closely packed nests, cell outlines were practically indistinguishable, the cytoplasmic masses appearing as syncytial structures in which the nuclei were hyperchromatic, but only a few mitotic figures were found. There was very little necrosis and hemorrhage.

Sections of the liver showed the characteristic picture of bile stasis with pigmentation of the hepatic and Kupffer cells in the inner portion of the lobules with associated degeneration and necrosis of the parenchyma and with congestion of the sinusoids. The portal radicles showed a marked increase in connective tissue and small bile duct proliferation and a low grade chronic inflammatory reaction. In one portion of the section there was a nodule of neoplastic cells resembling those described above.

There was no evidence of carcinomatous invasion of the pancreas, even in those areas attached to the portions of the duodenum in which there was neoplastic infiltration of its musculature. A low grade lymphocytic reaction and marked fibrosis were observed through the pancreatic tissue.

There were marked biliary pigmentation of the kidney and a moderate grade of nephrosis with congestion.

Case 12.—J. W., white, female, age 59, was admitted to the Jefferson Hospital, October 10, 1927, complaining of slight jaundice, belching, weakness, gastric distress, pain in the back and loss of 50 pounds (22.7 Kg.). She recalled having had occasional attacks of indigestion which were not associated with pain or jaundice; laterally, she had noticed some edema of the ankles, especially at the end of the day. Her terminal illness developed suddenly, in December, 1926, with symptoms suggestive of acute food poisoning followed by a persistent feeling of distress in the region of the stomach, which was accentuated by taking food. A month later, jaundice appeared and deepened progressively; the stools became clay-colored and remained light until two weeks before admission. At about this time she experienced persistent pain in the back, and there ensued a gradual enlargement of the abdomen.

Physical Examination showed the abdomen to be distended with fluid. It was extremely tender in the epigastric region. The edge of the liver was palpable 8 cm. below the costal margin in the midclavicular line. The gallbladder was not visualized in the roentgenologic studies. Fluoroscopic examination of the gastro-intestinal tract following a barium meal, January 21, 1927, showed rapid filling of the stomach but peristalsis was not active during the first few minutes. The fundus of the stomach was situated four fingers' breadth below the iliac crest. An elongated and dilated duodenal bulb was visualized and, although no defect of the bulb could be determined, it was felt that its configuration was suggestive of some pathologic change. *Clinical Diagnosis:* Carcinoma of the head of the pancreas or gallbladder disease. The patient became gradually weaker and died, October 19, 1927.

Autopsy.—Eight hours after death: Dr. B. L. Crawford. The combined gross and microscopic diagnoses were: (1) Peripapillary adenocarcinoma of the duodenum with extension into the pancreas and mesentery; metastases to the liver and lymph nodes; (2) marked dilatation of the extrahepatic bile ducts and calculous cholecystitis; (3) dilatation of the pancreatic ducts and chronic pancreatitis; (4) hemoperitoneum, originating probably from a rupture of the liver; and (5) chronic nephritis with arteriosclerosis.

The skin was pale and sallow but not definitely jaundiced; the peritoneal cavity contained 2,500 cc. of unclotted blood, and the greater part of the upper half of the abdomen on both sides was occupied by an enormously enlarged liver. The stomach was distended with greenish fluid.

At the papilla of Vater there was a soft, round, somewhat necrotic nodule in the wall of the duodenum which was elevated 2 cm. above the surface and measured 3 cm. in diameter. The common bile duct opened into the center of this nodule and bile could be expressed through the orifice, which readily admitted the passage of a probe all the way through into the gallbladder. The head of the pancreas was densely adherent to the duodenum opposite the lesion but, as far as could be ascertained, it was not extensively involved by tumor tissue. Many regional lymph nodes, in and behind the peritoneum and about the liver and pancreas, were firm, gray and enlarged. The liver weighed 3,970 Gm. and was firm, mottled, uniformly enlarged, and slightly nodular on the surface. On section, soft, gray nodules of tumor tissue were found to be embedded in a relatively small amount of residual hepatic tissue, which was firm, friable and hemorrhagic and cut easily. Beneath the capsule, in one area in the left margin, there was a rupture of the liver substance 2 cm. in length, which was considered the probable source of the hemoperitoneum. The gallbladder was thickened and contained a small amount of dark green bile together with several large, irregular, dark green calculi. A finger was readily introduced into the common bile duct up to its point of entrance into the mass surrounding the papilla of Vater.

Pathologic Examination.—The section of the duodenum consisted, at one end, of intestinal mucous membrane and underlying this a thick muscular wall which gradually tapered off and disappeared at the opposite end of the section. Beginning at the wide border and following along the surface of the section, the mucous membrane became gradually thicker, coincident with the development of a patchy malignant change in the form of nests of atypical epithelial cells in the deeper mucosa and submucosa. The lining of the intestine expanded into a broad papillary projection which, after partially encircling the narrowed end of the muscular coat, became atrophic, autolyzed and villous-like, and resembled the epithelium of the common bile duct. The neoplastic lesion consisted of nodules and large acini composed of papillary projections with relatively few cells embedded in considerable quantities of mucinous material. The underlying muscular coat was infiltrated with small clumps of columnar or polyhedral, acidophilic, vacuolated cells surrounded by slender basophilic mucinous strands. The nuclei were usually hyperchromatic, variable in size and shape, basally situated in the columnar cells and not observed in mitoses. The supporting stroma was relatively scanty and rather avascular.

The pancreatic tissue was infiltrated with tumor cells and showed dilatation of the ducts and extensive fibrosis. Metastatic lesions were observed in the lymph nodes, mesentery and liver, and showed infiltration of nerves and blood vessels and extensive hemorrhage and necrosis. The hepatic tissue was congested in the inner portion of the lobules and compressed and atrophied about the tumor nodules.

Case 13.—E. S., white, female, age 79, was admitted to the Philadelphia General Hospital, December 19, 1926. The onset of her illness had occurred six months previously with jaundice, clay-colored stools and itching, and later on, diarrhea, nocturia and inability to lie prone in bed. There was no history of weight loss.

Physical Examination showed a slight abdominal distention; on deep inspiration a small mass was palpable, which descended from the edge of the liver in the right upper quadrant of the abdomen. Roentgenologic studies of the gastro-intestinal tract disclosed

what was interpreted as the presence of a lesion extrinsic to the stomach and duodenum. *Clinical Diagnosis:* Carcinoma of the pancreas and bile ducts. Death occurred, December 26, 1926.

Autopsy.—Ten hours after death: Dr. F. W. Konzelman. The combined gross anatomic and microscopic diagnoses were: (1) Adenocarcinoma of the region of the papilla of Vater; (2) hydrohepatosis with marked jaundice; (3) dilatation of pancreatic ducts and chronic interstitial pancreatitis; (4) bronchopneumonia; (5) dilatation of heart with acute myocardial degeneration; (6) arteriosclerosis of aorta, coronary arteries and renal arteries, and (7) nephrosis.

The peritoneal cavity was bile-stained and contained a small amount of yellowish fluid. Upon opening the duodenum the papilla of Vater was found encircled by indurated

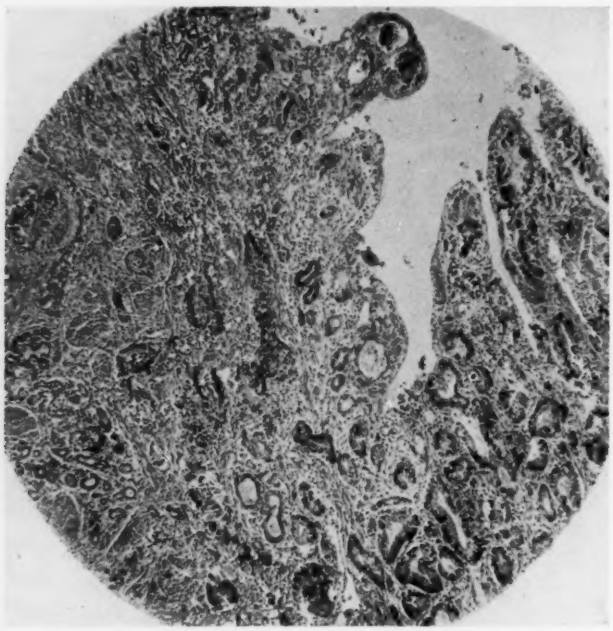


FIG. 6.—Case 13: Ampulla of Vater showing a malignant change in the tips of the villi. The atypical epithelial cells extend deeply into the wall of the duct. (×40)

tissue. There was no ulceration and the lesion involving the papilla did not project into the lumen of the intestine. The ampulla of Vater was apparently not examined. Proximally, the biliary passages were enormously distended and contained a large amount of watery, green bile. The liver, weighing 2,950 Gm., was tough and fibrous, and showed a finely granular green surface. The cut surface was mottled with fine green and yellow markings.

Pathologic Examination.—A section was obtained for histologic study which passed through the duodenum and included the ampulla of Vater. One side of the ampulla appeared normal except for autolysis of the epithelial lining cells. At one point a malignant change was observed in the tips of the villous projections and on the surface. Here the atypical epithelial cells were piled up forming a thick plaque without definite ulceration (Fig. 6). The tumor tissue extended through the wall of the duct into all coats of the surrounding duodenum, permeating, only slightly, however, into the autolyzed duodenal mucous membrane in its deepest portion. The neoplastic cells were well differentiated, tall columnar elements with acidophilic granular cytoplasm and basally situated nuclei. A few of the cells were irregular in size, shape and staining, and had enlarged hyper-

chromatic lobulated nuclei. Mitotic figures were infrequently observed and had a regular appearance. Most of the atypical cells were arranged in small round glandular structures but in places the acini were large and elongated with hyperplastic lining cells. In a few places the tumor cells grew in nests and irregular cords. The stroma was composed of mature connective tissue which was relatively scanty, avascular and infiltrated with small round cells and polymorphonuclear leukocytes, especially where the tumor tissue was necrotic.

The lungs showed bronchopneumonia, congestion and edema.

The pancreas showed dilatation of the ducts and diffuse and perilobular fibrosis. The parenchymatous tissue was somewhat atrophied, but the islands of Langerhans were well preserved and there were practically no inflammatory cells.

The kidneys showed a moderate grade of nephrosis and slight bile pigmentation.

The liver showed the well advanced changes of biliary stasis with pigmentation and degeneration in the inner portion of the lobule, focal midzonal necroses, proliferation of the small bile ducts, fibrosis of the portal radicles and marked associated inflammatory reaction.

Case 14.—W. H., colored, male, age 77, was admitted to the Philadelphia General Hospital, November 11, 1926, with marked jaundice. The only history obtainable was that the patient had been sick for two years with indefinite epigastric pain, weakness and loss of weight. The exact time at which jaundice appeared could not be determined.

Physical Examination showed a large, tender, immovable mass, palpable in the epigastrium just below the costal margin and a little to the right of the midline. The patient was found dead in bed, November 14, 1926.

Autopsy.—Twenty-four hours after death: Dr. E. Wiess. The combined gross anatomic and microscopic diagnoses were: (1) Peripapillary adenocarcinoma of the duodenum with extension to the pancreas; (2) hydrohepatosis with suppurative cholangeitis and marked jaundice; (3) obstruction to the duct of Wirsung and chronic pancreatitis; (4) myocardial degeneration; (5) arteriosclerosis of the kidneys with bile pigmentation and nephrosis; and (6) fibrocaseous tuberculosis of the lymph nodes.

The stomach was dilated and contained bile-stained, slimy mucus. The site usually occupied by the papilla of Vater was marked by an elevated, ulcerated, congested lesion which was directly continuous with a large tumor mass in the head of the pancreas. Proximal to the lesion, the duct of Wirsung and the biliary passages were enormously distended. The gallbladder measured 16x8 cm. and was filled with milky fluid. The intrahepatic biliary ducts were distended and the liver was tense and finely mottled. Many of the regional lymph nodes were firm and white.

Pathologic Examination.—There were areas of acute inflammation and ulceration in the mucous membrane of the duodenum. Atypical epithelial cells supported by a moderate amount of stroma blended in places with the mucosal cells and extended into the deeper layers of the section. For the most part they were arranged in small, round or larger, irregular acini, a few of which resembled crypts of intestinal mucosa in having a single layer of tall columnar epithelium with deeply placed polar nuclei. Generally, however, the cells were poorly differentiated, of irregular shapes and varying sizes and tended to be massed into nests. The nuclei were oval, round, large and irregular; many of them were hyperchromatic and contained prominent nucleoli and a few were seen in mitosis. The tumor was vascular, with many immature blood vessels. There were large areas of hemorrhage, necrosis and suppuration, especially near the surface. The deeper portion of this section was continuous with a large, necrotic tumor mass in which pancreatic tissue was not identified.

A section of pancreas contained several dilated ducts which were lined by irregular tall columnar epithelium thrown into small folds. There was marked atrophy of the parenchymatous tissue of the pancreas and a diffuse proliferation of fibrous tissue markedly infiltrated with lymphocytes. The islands of Langerhans survived the atrophic process and appeared to be relatively numerous.

The liver showed marked bile stasis, with the usual pigmentation and necrosis in the inner portion of the lobule, biliary and focal midzonal necroses and bile duct proliferation, fibrosis and marked chronic suppurative inflammatory reaction in the portal areas.

The kidney showed bile pigmentation and a moderate degree of nephrosis.

Section of a lymph node showed extensive, fibrosing miliary tuberculosis. Sections of the lung were not available for study.

Case 15.—J. M., white, male, age 46, was admitted to the Philadelphia General Hospital, May 22, 1933, after an illness of two months' duration. At the onset there were cough, loss of appetite and edema of the extremities; ten days before admission, jaundice and clay-colored stools and a loss of 20 pounds in weight (9 Kg.) were noted.

Physical Examination showed abdominal distention and a palpable mass in the right upper quadrant, with fulness and resistance over the gallbladder area. Following the removal of 3,300 cc. of dark, amber fluid from the peritoneal cavity, several nodules became palpable in the right upper quadrant. Roentgenologic studies revealed the contours of the stomach normal in the erect position with slight displacement of the organ to the right. Peristaltic movements passed uninterruptedly along both curvatures. The cap appeared normal, but there was widening of the duodenal loop and considerable stasis in the second and third portions. There was no evidence of metastatic deposits in the lungs. The roentgenologic conclusion was that the stomach and duodenum were negative. The icterus index was 50 and 60, respectively, on two occasions. There was a biphasic van den Berg reaction and 3.5 mg. of bilirubin per 100 cc. of blood. The patient developed paranoid delusions and died, June 12, 1933.

Autopsy.—Twenty-two hours after death: Dr. H. Lund. The combined gross anatomic and microscopic diagnoses were: (1) Carcinoma of the ampulla of Vater with extension through the wall of the duodenum into the pancreas; (2) suppurative hydrohepatosis with marked jaundice; (3) obstruction and suppurative inflammation of the duct of Wirsung with chronic pancreatitis and peripancreatic fat necrosis; (4) bronchopneumonia; and (5) renal arteriosclerosis and marked nephrosis.

There was moderate distention of the stomach and proximal half of the duodenum. The papilla of Vater consisted of a smooth, light yellow, fluctuant nodule which projected for a distance of 1 cm. into the lumen of the duodenum. The immediately surrounding tissue was quite firm. The orifice of the common bile duct was situated on the under surface of this nodule near its junction point with the duodenal mucosa. A probe was readily passed into the ampulla which, when opened, disclosed the presence of a small, pink polypoid lesion projecting 0.15 cm. above the level of the mucous membrane. Proximal to this lesion the common bile duct was dilated to a diameter of 3.6 cm.; the gallbladder formed a greatly distended, thin-walled sac measuring 16x7x45 cm., and contained flaky yellow fluid.

The liver weighed 1,700 Gm.; it was firm, green, cut with increased resistance and disclosed marked distention of the intrahepatic bile ducts. Small, yellow flake-like areas, 2 cm. in diameter, were observed in the hepatic parenchyma near the hilus.

The pancreas was much firmer than normal and cut with increased resistance, disclosing marked distention of the duct of Wirsung throughout its entire course. This duct measured 2.5 cm. in the tail of the pancreas and 3.5 cm. in the head.

Pathologic Examination.—The small polypoid nodule observed in the ampulla of Vater consisted of cells in disorderly arrangement but tending to form crypts and acini (Fig. 7.), The nuclei varied in size and shape, some attaining a very large size. They showed some evidence of biliary autolysis but in spite of this stained more intensely basophilic than would be expected. No mitotic figures were observed. The atypical epithelial cells were supported by a central stroma consisting of a few strands of fibrous tissue which branched near the base to form a polyp consisting of two small finger-like processes. The base merged at right angles into a zone of smooth muscle with no characteristic arrangement. The epithelial cells described above penetrated in small strands and clumps into this muscular tissue.

The common bile duct was markedly thickened and its mucosa was autolyzed and stained with bile. No evidences of carcinoma were observed.

The duodenum had a moderately hyperplastic mucosa; its muscular wall was thickened and in the deeper portions, strands of small atypical epithelial cells, tending to be arranged in single layer rows, penetrated between the bundles of smooth muscle from the side opposite the mucosa.

A section of the pancreas adjoining the common bile duct showed similar small atypical epithelial cells arranged in rows a single layer deep. These cells tended to be polyhedral, formed elliptical acini, and closely resembled the cells in the ampullary polyp

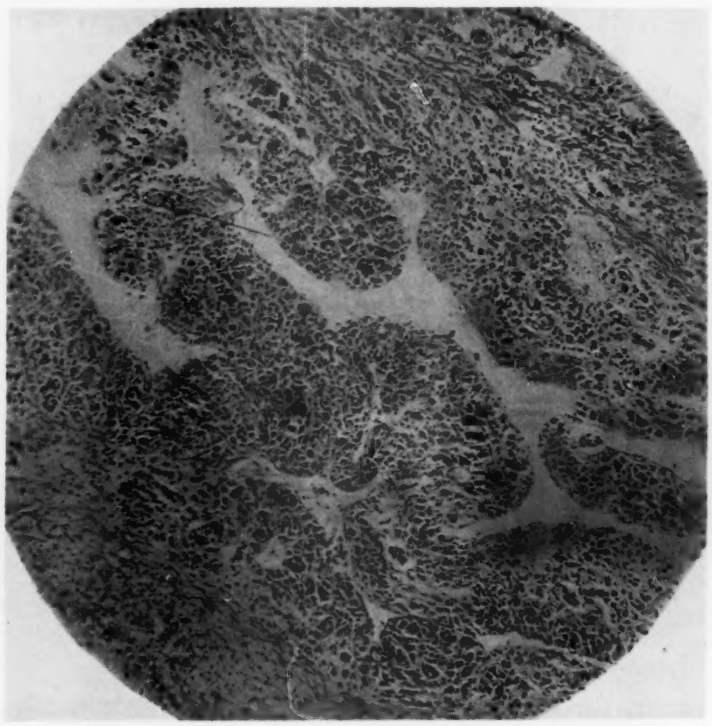


FIG. 7.—Case 15: Lumen of ampulla of Vater almost filled with broad papillary projections of the malignant polyp with infiltration of the surrounding tissues. (×100)

without, however, showing as much variation in the size of the nuclei. Sections from various other portions of the pancreas showed parenchymal atrophy, interstitial fibrosis and suppurative inflammation of the ducts.

The liver showed characteristic evidences of long-standing obstruction, with pigmentation, degeneration and atrophy of the cells about the central and sublobular veins, biliary and focal midzonal necroses and marked fibrosis about the portal radicles. The sinusoids were distended and there were numerous small abscesses observed near the portal radicles and beneath the capsule of the liver. The hepatic parenchyma showed only slight evidences of regeneration and no mitotic figures.

Case 16.—G. P., white, female, age 45, was admitted to the Jefferson Hospital, August 9, 1937, complaining of itching, jaundice, pain in the back and loss of weight. The patient had always been in good health until seven weeks previously when she had generalized itching and slight chills. Jaundice appeared two weeks later with very dark urine and clay-colored stools. At this time, there was also pain in the lower thoracic

region of the back and a feeling of soreness in the right upper quadrant of the abdomen. The pain increased in severity, becoming continuous and, at times, there was radiation to both shoulder blades. Nausea and vomiting occurred on several occasions. The jaundice deepened progressively although, during the last two weeks, the stools had become brown and jaundice had diminished somewhat in intensity. The appetite was poor and there was a loss of 25 pounds (11 Kg.). The temperature was septic in type and varied from 99.5° to 104° F.

Physical Examination demonstrated a firm, irregular, tender mass which descended on inspiration to the level of the umbilicus, and which occupied the epigastrium and right upper quadrant of the abdomen. The duodenal content was blood-tinged and contained a small quantity of bile on the first examination; one week later, however, it had become bloody and did not show any bile on two examinations. The gallbladder was not visual-

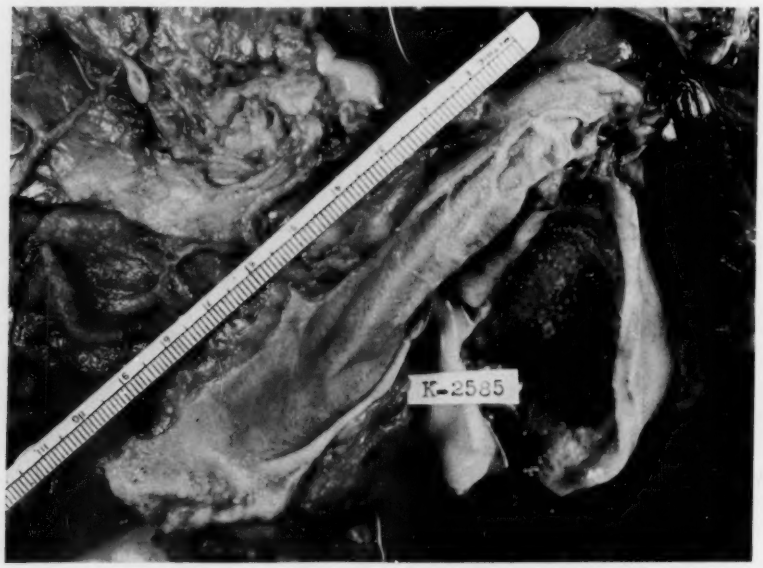


FIG. 8.—Case 16: Opened papilla of Vater and common bile duct. Note the granular, polypoid lesion in the terminal 1.3 cm., and the widely dilated ducts and gallbladder. (×1.5)

ized in the cholecystographic studies. Roentgenologic studies of the gastro-intestinal tract showed a normal stomach and duodenum and no abnormal retention of barium. The van den Bergh reaction on the blood was positive direct with 14 mg. per cent of bilirubin. Test of liver function with bromsulfalein showed 100 per cent retention of the dye in 30 minutes (2 mg. dosage).

On August 22, 1937, the patient vomited dark blood and passed several tarry stools. Bleeding from the gastro-intestinal tract continued. The course of the disease was increasingly downward, in spite of blood transfusions, totaling 2,500 cc. during the following six days. *Clinical Diagnosis:* Impacted stone in the common bile duct or carcinoma of the head of the pancreas. Death occurred, August 29, 1937.

Autopsy.—Ten hours after death: Dr. M. M. Lieber. The combined gross and microscopic diagnoses were: (1) Adenocarcinoma, primary in the region of the ampulla of Vater, with extension to the head of the pancreas and metastases to liver; (2) hydrohepatosis with marked jaundice; (3) obstruction of the duct of Wirsung with chronic pancreatitis; (4) biliary pigmentation of the kidney and moderate nephrosis; (5) bronchopneumonia; (6) acute myocardial degeneration and sclerosis of mitral and aortic valves; and (7) atherosclerosis of coronary arteries and aorta.

The stomach was distended with 250 cc. of fluid and partially digested food rem-

nants. The intestinal tract contained free blood and blood-tinged mucus. The proximal segment of the second portion of the duodenum was densely adherent to the hilum of the liver. The papilla of Vater projected into the duodenum as a soft, cylindro-conical body 3 cm. long and 2.5 cm. in diameter. A probe easily passed through the orifice on the apex of the papilla and was followed by a flow of greenish-black bile. The intestinal mucous membrane covering the papilla was smooth, not thickened and freely movable. On opening the bile ducts and papilla of Vater, a sharply demarcated, soft, granular polypoid lesion, without ulceration, was found in the terminal 1.3 cm. (Fig. 8). The orifice of the duct of Wirsung was obscured; retrograde probing of the dilated duct met with an absolute obstruction in the head of the pancreas adjacent to the primary lesion. The duct of Santorini was patent and opened into the duodenum 2 cm. proximal to the papilla of Vater. Proximal to the primary lesion, the biliary ducts and gallbladder were moderately distended. The regional lymph nodes were slightly enlarged and soft and did not appear to contain any neoplastic tissue.

The gallbladder projected 3 cm. below the inferior margin of the liver and was filled with 60 cc. of greenish-black bile; no calculi were found; its wall was moderately thickened.

The liver weighed 2,000 Gm. The surface was smooth except for varicosed biliary ducts and two small, circumscribed, yellowish-gray metastatic nodules in the right lobe. The cut surface was grass-green and the biliary ducts were markedly distended and filled with green bile.

The pancreas was firm and cut with a grating sensation, disclosing perilobular fibrosis, fatty infiltration and atrophy of the parenchyma. There were no evidences of neoplastic infiltration into the head of the organ.

The kidneys were slightly enlarged and the cut surfaces yellowish-green. Intense green streaking was noted at the apices of the pyramids and the cortices appeared slightly swollen.

Pathologic Examination.—A number of sections for microscopic study were obtained by making longitudinal incisions through the opened common bile duct and included the terminal portion of the latter, the ampulla, and papilla of Vater, the adjacent duodenum and underlying pancreas. In the ampulla, the zone of malignant transformation was abrupt, and characterized by enlargement of the acini in its wall with a heaping up of cylindrical and cuboidal cells into multiple layers. These acini extended to the surface and were followed by the formation of short, plump, villous projections. Approaching the papilla, these villous structures appeared as long, slender, finger-like projections consisting of atypical cuboidal and polyhedral cells scattered irregularly in a fine, fibrillar stroma capped by masses of these cells so that many of them appeared knob-like. The tumor cells extended into the muscularis and submucosa of the duodenum, covering the papilla of Vater; the duodenal mucous membrane, however, did not show any involvement in any of the sections examined.

The atypical epithelial cells were well differentiated, for the most part, and occurred as cylindrical, columnar or cuboidal elements. The nuclei were basally situated in the cells and stained fairly uniformly, only a few showing hyperchromasia. Mitotic figures were rarely observed. The majority of the tumor cells were arranged in the form of irregular acini lined by a single layer of cells and occasionally by eccentric multiple layers. The stroma was generally abundant and not very vascular. Many polymorphonuclear leukocytes were irregularly scattered through the mucosa and submucosa of the duodenum covering the papilla of Vater, and they occurred in lesser numbers in the stroma of the neoplastic tissue.

The immediately adjacent portion of the pancreas, underlying the ampulla of Vater, showed marked perilobular and interacinar fibrosis with atrophy of the parenchyma and, in one section, three small tumor acini were found extending into the interstices of a pancreatic lobule. A large branch of the pancreatic duct appeared dilated but its mucous membrane was normal.

The liver showed marked biliary pigmentation, slight degeneration in the inner portion of the lobule and slight fibrosis and moderate bile duct proliferation in the portal radicles. A small metastatic nodule, beneath the capsule of the liver, consisted of irregular, small acini having the characteristics of the primary lesion.

The kidneys showed slight biliary pigmentation and a moderate grade of nephrosis.

Case 17.—E. F., white, female, age 62, was admitted to the Jefferson Hospital, November 14, 1937, complaining of painless jaundice, generalized itching, belching, flatulency, constipation, epigastric soreness and loss of weight. The onset had occurred six months previous to admission. The first complaint had been a substernal sense of suffocation, especially after eating and on effort. Constipation was also noted at this time. About one month later, jaundice appeared associated with generalized itching and clay-colored stools. There was no pain at any time; later, however, she developed a sense of midepigastric soreness, especially in the evening. Belching and flatulency had occurred irregularly from the onset. There had been a loss of 27 pounds (12.2 Kg.) during the past six months. Nausea, vomiting, diarrhea and melena were not noted at any time.

Physical Examination showed a slight fulness and a definite sense of resistance in the right hypochondrium. The liver edge was sharp, firm, smooth, not tender, and extended four fingers' breadth below the costal margin. The gallbladder was not palpable and no masses could be detected. Roentgenologic studies of the gastro-intestinal tract showed slight broadening of the duodenal curve with delay in the passage of barium through the second and third portions of the duodenum, interpreted as suggestive of some enlargement of the pancreas. Cholecystographic studies showed nonvisualization of the gallbladder. Tests of hepatic function, performed on the second day, resulted in a positive van den Bergh reaction with 10.8 mg. per cent of bilirubin; an icterus index of 61; and a retention of 40 per cent of bromsulfalein in 30 minutes (2 mg. dosage); seven days later, the quantitative van den Bergh test showed 7.44 mg. per cent of bilirubin and 20 per cent retention of bromsulfalein in 30 minutes. *Clinical Diagnosis:* Carcinoma of the head of the pancreas or primary carcinoma of the liver.

Operation.—November 24, 1937: Dr. George P. Muller. Celiotomy disclosed an enlarged, smooth and jaundiced liver. The gallbladder and common bile duct were markedly dilated. The former was aspirated and its fundus anastomosed to the lesser curvature of the stomach. A curette introduced into the common bile duct met with an obstruction in the region of the papilla of Vater, and a small quantity of soft, friable, gray tissue was withdrawn. The common duct was ligated. The stomach was anastomosed to the jejunum and two loops of jejunum were brought together and anastomosed. *Postoperative Diagnosis:* Carcinoma of the ampulla of Vater. On the second day postoperative, the temperature was normal and the pulse was strong and regular. The intensity of jaundice had diminished somewhat; on the evening of the third day, however, the urinary output decreased markedly, the temperature suddenly rose to 107° F. and death ensued.

Autopsy.—Nineteen hours after death: Dr. M. M. Lieber. The combined gross and microscopic diagnoses were: (1) Adenocarcinoma, primary in the region of the ampulla of Vater; (2) obstruction of common bile and pancreatic ducts; (3) generalized jaundice; (4) bile pigmentation and acute degeneration of kidneys; (5) acute myocardial degeneration; (6) biliary stasis and necrosis of liver; (7) hypostatic congestion of lungs with left-sided pleural effusion; (8) recent surgical anastomoses of gallbladder to stomach and jejunum; and (9) hemorrhage into the gastro-intestinal tract.

The stomach was markedly distended and contained 600 cc. of bile mixed with blood; the mucous membrane was atrophied. The proximal segment of the duodenum was moderately dilated. The papilla of Vater formed a cylindro-conical body 2.2 cm. long and 1.5 cm. in diameter. The duodenal mucous membrane was smooth and freely movable over all portions of the papilla. The orifice on the apex of the papilla was moderately dilated. On longitudinal section, a gray, soft, friable, granular polypoid lesion 1.5 cm. in length, and completely annular, was disclosed within the papilla. The orifice of the duct

of Wirsung was obscured by the primary growth. In the body of the pancreas, the duct was dilated and measured 4 cm. in circumference. Retrograde dissection of the duct of Wirsung showed it to be completely obstructed by the tumor mass in the ampulla of Vater. A number of miliary, gray nodules studded the inner lining of the duct near its orifice. The duct of Santorini emptied into the duct of Wirsung, 1.5 cm. proximal to the latter's entrance into the ampulla. The common bile duct, proximal to the primary lesion, was moderately distended and its wall hypertrophied.

The liver weighed 1,250 Gm. It cut with slightly increased resistance and the surface was predominately yellow with a slight admixture of green. Small, pin point focal gray areas were scattered through the parenchyma. The larger biliary ducts contained a muddy-yellow fluid while the smaller ducts were dilated and filled with dark green bile.

The pancreas was firm and showed no evidence of extension of the neoplasm into it.

The kidneys were enlarged, bile-stained and showed a marked degree of nephrosis.

The large intestine was widely dilated and filled with liquid and clotted blood.

Microscopically, longitudinal sections taken through the opened papilla of Vater and including the ampulla of Vater, common bile duct and a portion of the underlying pancreas, showed no evidence of neoplastic change in the autolytic duodenal mucosa covering the outer surface of the papilla of Vater. The submucosa was also free of neoplasm except in one small area. The muscular layers of the duodenum were, however, infiltrated with large acinar structures lined by tall cylindrical cells often heaped up to form papillary spurs. The inner surface of the papilla was lined by long, slender, branching processes consisting of narrow cores of fibrillar, vascular connective tissue covered by single or multiple layers of cylindrical cells. In the ampulla, these processes were plumper and shorter and finally appeared as half-moon-shaped nests of flattened cells. In the depths of the tissue, small and large acini were present, the lumina of many of the latter being filled with a homogeneous, eosinophilic substance in which desquamated cells and débris were also present. Similar new formations were also observed in sections of the wall of the duct of Wirsung in its proximal portion. Small acini projected above the adjacent normal mucous surface of the inferior wall of this duct. The underlying pancreatic tissue was separated from the main tumor growth by a band of loose connective tissue which was free of neoplasm. The neoplastic cells were generally well differentiated into tall cylindrical elements with basally situated nuclei showing considerable variation in size, shape and staining; mitotic figures were rarely observed. There was little or no tendency for the cells to grow in the form of clumps, cords or nests. The supporting stroma was scanty, vascular and without appreciable inflammatory cell reaction.

Sections of pancreas showed dilatation of ducts, extensive interlobular and interacinar fibrosis with consequent atrophy of the parenchyma and little or no evidences of inflammation.

The liver showed varying degrees of involvement with necrosis of the inner one-half to two-thirds of the lobules and focal midzonal and biliary necroses. The amount of biliary pigment was small. The characteristic changes associated with decompression of obstructed biliary passages, previously described by us (Stewart and Lieber), were clearly illustrated in this case. These consisted of disruption of intralobular architecture with disorganization and dissociation of hepatic cell cords and atrophy and distortion of the hepatic cells. These changes were particularly pronounced about the larger portal radicles. Hypertrophy, hyperchromasia, binucleation and multinucleation of cells at the peripheries of the lobules indicated regeneration of hepatic cells, but mitotic figures were not observed. There was a marked proliferation of the smaller biliary ducts associated with a pronounced increase in the connective tissue which was periportal, interlobular and perilobular in distribution, and a slight infiltration of lymphocytes and monocytes.

The kidneys contained little or no bile pigment and cortical regressive changes were only moderate in degree.

TO BE CONTINUED

NEUROFIBROSARCOMA OF THE SMALL BOWEL

REPORT OF TWO CASES

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RECOGNITION of neoplasms derived from the nerve trunks is usually credited to von Recklinghausen,[2] in 1882; however, Kölliker, in 1860, and numerous others[1] had described the disease previously. The literature offered covers more than a century and, even so, the most recent papers indicate that there still is no uniformity of opinion as to classification and histogenesis. Therefore, any historic review is erroneous, for it is impossible to accept all examples offered as the same type of growth, and many descriptions are not sufficiently clear to permit analysis. It seems quite evident that the fibromata and fibrosarcomata were a composite group which is now being subdivided.

The name, neuroma, is perhaps the oldest one and was used by the writers contemporary with von Recklinghausen, but there are many aliases, each of which was offered as descriptive of structure or specific origin. These include neurilemoma, neuronoma, peripheral fibroglioma, fibroblastoma, neurogenic fibroma, neurinoma, neuroma, peripheral glioma, lemmoma, schwannoma, false neuroma, and perineural fibroblastoma.

These tumors have been found in almost all parts of the body, but they predominate in the skin. It is said[1] they may occur in the digestive tract at any point from the "lips to anus." Many are described in the stomach, a few in the colon, one in the appendix, and a few in the small bowel.

Some of the earliest reports indicate that these tumors in various locations are sometimes malignant. Von Recklinghausen[2] described a malignant one in the jejunum. Adrian,[3] Delagéniére,[4] Denecke[5] each reported one in the duodenum. Lemonnier and Peycelon,[6] Dudley,[7] Konig[8] and Leriche[9] reported one case each, and Norlander[10] describes three cases in the jejunum and ileum. Case reports of neurofibrosarcoma of the small bowel include three in the duodenum and eight in the remaining portion. Most of these were multiple tumors.

Etiology.—The tumors usually appear during middle age, and they are about equally divided between the sexes.

It is suggested by Masson[11] that trauma or inflammation of the nerve trunks is a possible etiologic factor. He produced tumor growths of nerve trunks in animals by transplanting sections of a peripheral nerve to prevent the axone from coming in contact with the cells of the nerve sheath. It seems the cells of the sheath of Schwann begin to proliferate as soon as degeneration of the axone is well advanced, but this ceases immediately if the regenerating axone enters the sheath. If the neurite is prevented from

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entering the sheath, the cells would grow as long as the observations were continued, which was five months. The structure of these proliferating sheaths of Schwann is identical with that of the neurofibroma. However, it is yet to be proved that neoplasia and hyperplasia are identical; in fact, there is much evidence to indicate that continuous growth is a minor or incidental characteristic of neoplasms.

These growths were considered as developmental by Warthin (quoted by Case[12]). This is also suggested by others,[13] who pointed out the association of malformations in some patients with neurofibromata. It seems quite clear that fetal rests may be the origin of neoplastic tissue, but there is very little evidence to indicate that the neoplastic characteristics of tissue are dependent upon faulty development. It is evident that certain carcinogenic agents, the roentgen ray for instance, can bring about neoplastic changes in any or all cells of certain tissues, the squamous epithelium of the skin, for example.

The specific etiology will, therefore, remain obscure until the day when the mechanism of neoplastic development will have been explained.

Histogenesis.—The structure of the nerve trunk is uniformly described. Briefly, it consists of nerve cell processes, the axones, which may or may not have a myelin coat but are covered by the neurilemma, or sheath of Schwann. These are supported by a delicate framework of connective tissue, the endoneurium. Small groups of nerve fibers with their supporting endoneurium are grouped into strands or funiculi which are surrounded by connective tissue, the perineurium, and these funiculi are also grouped in strands, the nerve trunk, which is supported and surrounded by connective tissue, the epineurium. There are two possible sources, excluding the vessels, of neoplastic growth, the supporting connective tissue and the neurilemma.

Concerning the development of these structures there is also uniform agreement. The connective tissue elements, the epineurium, perineurium, and endoneurium are, like other connective tissue elements, mesodermal in origin. The two remaining elements, the sheath of Schwann, or neurilemma, and the nerve cell processes, are derived from epithelium, the ectoderm, and have a common ancestry in the cells constituting the neural plate. The neurilemma cells grow with the nerve cell processes as they penetrate the tissues during development.

Concerning the histogenesis of neurofibromata there are three points of uniform opinion: First, that neoplasms do develop from the nerve trunk; second, that axones are sometimes found in them, but they are only accidental, and are remnants of the invaded and deranged nerve trunk in which the growth developed; they do not grow; and third, they contain no nerve cells.

Concerning the remaining important point, the mother cells, there is much controversy. It was contended recently by Penfield,[14] and previously by many others,[13] that the parent cells are those of the connective tissue

elements of the nerve trunks. It would follow that such names as fibroma or perineural fibroblastoma are representative.

It has also been suggested[15] that the tumors are connective tissue but derived from the neurilemma cells by metaplasia. This involves a change from one primary tissue (nerve) to another primary tissue (connective), which perhaps never occurs except in embryonic life and neoplastic development.

Another opinion is that neoplasms do develop from the cells of the neurilemma, and it follows that such names as neurilemoma, peripheral glioma, and schwannoma are correct. This view is supported by Masson[11] and many others,[13] among whom are Vorocay, Pick, and Bielschowsky, who report having seen microscopic neoplasms in which the cells could be traced by continuity to the cells of the neurilemma. Others avoid the controversy by suggesting that any one or both elements of the nerve trunk may be the parent tissue of the neoplasm. And for this interpretation, practically all the evidence presented in argument can be accepted.

The question is not merely academic. Its solution and the specific classification of the growths will quite certainly lead to more accurate prognosis and treatment. In fact, the controversy was initiated by the observation that all fibromata did not behave alike. It seems that the weight of evidence is rapidly accumulating in favor of the theory that the neurilemma is the parent tissue for a rapidly growing list of neoplasms, and that the accepted list of pure fibromata is getting smaller and smaller.

Characteristics.—The malignant growths are like the benign in that they are more often multiple than solitary. The tumor mass is usually spherical or modified spherical, with a connective tissue capsule. If there is no covering, there is a pressure atrophy zone about the mass and diffuse infiltration at the border is lacking. The more malignant ones are soft and friable, somewhat resembling brain tissue. Firmness is increased in proportion to the amount of connective tissue stroma, so that some specimens are hard, but those that are so described are usually benign. The color is gray, and again is similar to that of the brain. Frequently there are yellow areas, necrosis, and black or blood red areas because of hemorrhage. Lobulation is definite except in the most malignant growths. Commonly there are cavities containing grumous material consisting of necrotic tissue and blood, the proportion of blood modifying the color. The wall of the cavity is irregular and friable.

The cells are elongated, stellate, or in localized areas, polygonal. Mitotic figures are present and some are atypical. Small giant cells may be present. The cytoplasm stains with eosin, but often has a blue quality. There are coarse processes which are blue in phosphotungstic acid hematoxylin preparations. There is a varying amount of fibrillar substance which is collagenous in its behavior to stains. The cells are arranged in interlacing bundles and sometimes in whorls. Palisading is present in some specimens, and if so,

is considered by Masson[11] to be pathognomonic. Often there are imperfectly organized spherical arrangements that are interpreted as aborted attempts at Meissner corpuscle formations. It has been suggested that these formations, the palisades, and the clinical observation that motor paralyses seldom occur, are evidence that the growths have occurred on sensory nerves; that those which do occur on motor nerves have no palisades or imperfect corpuscles. If this reasoning is correct, it may explain the infrequency of neurofibromata in the gastro-intestinal tract, since its sensory nerve supply is meager. The stroma is very small in amount in the malignant ones. The blood vessels are usually numerous, very large, and have thin imperfect walls so that hemorrhage is common and considerable. There may be large blood-filled spaces lined by endothelium supported by only a few connective tissue cells. There is infiltration at the periphery of the growth, but displacement is more prominent. They may be myxomatous. Axones are not found in the malignant tumors.

The grade of malignancy is not high. Stewart and Copeland,[13] in reporting 73 cases, none in the intestine, divided them into Grades I, II and III, placing none of the specimens in Grade IV. There are no reports of grading the intestinal tumors, and the subsequent histories of these reported are too inadequate to be of value.

Metastases are not common but have occurred in the regional lymph nodes, the liver, and the diaphragm.[16] Metastasis to the skeleton has been observed in two instances[17] of malignant peripheral tumors.

Judging from the records, some tumors are malignant at the onset, but von Recklinghausen considered his case as one of a change from benign to malignant because there were other benign tumors in the intestine. Peripheral tumors in which malignant change occurred have been observed.

Clinical Aspect.—A number of the patients with neurofibrosarcoma of the small bowel have had neurofibromatosis, or von Recklinghausen's disease, for years. In others, there were no peripheral lesions demonstrable. The absence of nerve tumors is difficult to determine, however, since they may be on the deep, large nerve trunks and very small.

The symptoms are usually those of obstruction, either sudden or gradually progressing. Usually the tumor is large enough to be palpated.

Prognosis.—The group of case reports is too small and incomplete to be of much aid in determining prognosis. The same tumor in other locations has a poor prognosis, the five-year cases reported by Stewart and Copeland[13] being 25 per cent in Grade I, 5½ per cent in Grade II, and 5 per cent in Grade III. If they are multiple, and they are more often than not, resection may be impossible for that reason alone. Since the grade of malignancy is not high, and metastases not common, it seems that resection of the bowel with the tumor would offer a good prognosis if the tumor is solitary.

The first case is that of a solitary lesion springing from the wall of the jejunum opposite the mesenteric attachment.

CASE REPORTS

Case 1.—H. C., female, age 72, white, married, was admitted to the hospital July 27, 1937, presenting an abdominal tumor. The patient had been apparently well until two years previously, at which time she began to experience a feeling of distress and a sense of fulness low in the abdomen. She developed backache and frequency of urination which during the past six months has been decidedly exaggerated, and within this time she had noticed enlargement of the abdomen. Her past and family histories are entirely negative. She has had eight children, varying in age from 30 to 13. During the past year she had noticed some shortness of breath on exertion and some swelling of the ankles at night.

Physical Examination.—The patient was somewhat thin but not acutely ill. The head, chest and extremities were entirely negative. There were no nodules either in

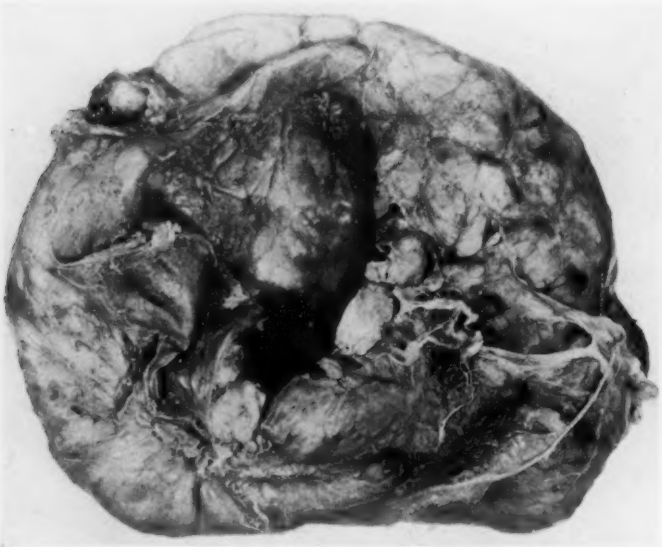

FIG. 1.—Case 1: Photograph of neoplasm. The small pedicle of attachment is at the lower left and the adherent omentum at the lower right. The large cavity was filled with necrotic tumor tissue and blood.

the arms or legs or any areas of pigmentation. Blood pressure 200/110. There was a distinct fulness in the lower abdomen extending mostly to the right side. Over this area there was dulness to percussion. This fulness or mass extended from the symphysis to about one and one-half inches above the umbilicus; it was soft and apparently fluctuant. The flanks were tympanitic. The upper abdomen was soft, relaxed and contained no masses. The liver was not enlarged nor was the spleen palpable. Pelvic examination revealed a relaxed perineum, normal cervix, and a tumor mass which filled the culdesac and was apparently continuous with the mass in the abdomen, extending up to about one and one-half inches above the umbilicus. Definite fluctuation could be obtained.

Urinalysis was negative other than for a trace of albumin. R.B.C. 3,620,000, Hb. 74.6 per cent. W.B.C. 10,350, with 92 per cent neutrophils, 1 per cent monocytes and 7 per cent lymphocytes. Kahn and Wassermann tests were negative. *Preoperative Diagnosis:* Right ovarian cyst.

Operation.—On opening the abdomen, a mass presented which extended from the pelvis almost to the costal margin. The left side of the mass seemed cystic and had the appearance of a gangrenous cyst wall such as is seen in twisted ovarian cysts. On the right side, however, this cyst was apparently continuous with some tissue which had the

appearance of brain. While separating the adhesions between this tumor and the pelvic organs, a gush of old blood, together with some necrotic tissue resembling broken-down carcinoma, was encountered. It was found that there was no attachment of this tumor to the pelvic organs except by very fine, fresh adhesions which were easily separated without bleeding. The omentum was adherent to the upper part of the tumor and was divided between ligatures. It was then found that the tumor was densely adherent to, or sprang from, a loop of jejunum in the upper left abdomen. It being impossible to separate the mass from this piece of intestine, a clamp was placed about the pedicle in the long axis of the bowel, and the tumor, together with the wall of the jejunum, was cut away. The opening in the jejunum was then closed and inverted with linen sutures.

A thorough inspection of the abdomen revealed that there had been some adhesions between the tumor and the peritoneum of the right lateral wall of the abdomen at about the level of the anterior-superior spine. Furthermore, there had been some adhesion to

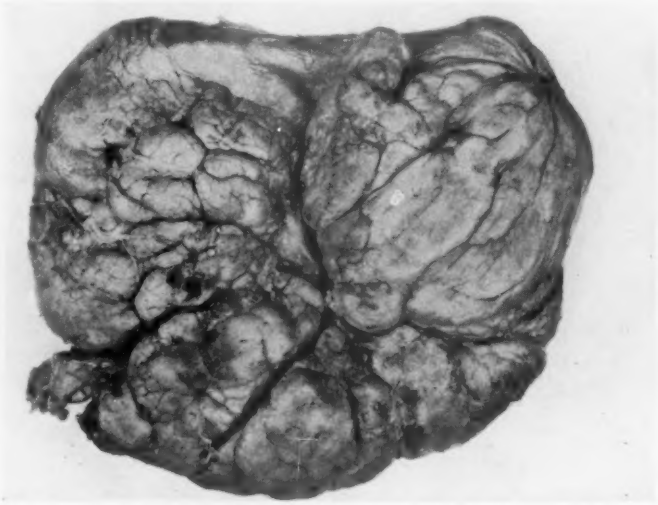

FIG. 2.—Case 1: Photograph of opposite side of attachment of tumor mass. There are deep fissures dividing the tumor into irregular lobules. The color is light gray; consistency soft.

the peritoneum above the bladder. Otherwise, the tumor was apparently free except for its attachment to the omentum and to the jejunum. The pelvic organs were normal. There were no nodes in the mesentery of the jejunum. The liver was of normal size, soft, and contained no metastatic nodules nor were any nodules evident in the spleen. The gallbladder contained no stones; the stomach was normal.

Pathologic Examination.—Gross: The specimen is a neoplasm in the shape of a flattened sphere and measures 28 cm. in greatest diameter. It has a small area of attachment, evidently by a pedicle, about 2x4 cm. Near this a small portion of the great omentum is adherent. The surface covering is thin peritoneum in which there are many large vessels. The contour is marked into irregular lobule formations by wide, shallow fissures. The mass has been opened near the pedicle and the content, which was necrotic tumor tissue and blood, has escaped, leaving a shell 1 to 3 cm. in thickness. The tissue is very friable, grayish substance without striations (Figs. 1 and 2).

Microscopically, sections show very dense parenchyma with almost imperceptible stroma. The cells are arranged in bundles that extend in all directions, and also in whorls. The cytoplasm is moderately abundant and extends in wide and coarse prolongations. There is a small amount of fibrillar intercellular substance. The nuclei have large chromatin granules, large true and false nucleoli, and a few are vesicular. There

is an occasional mitosis. Phosphotungstic acid stains reveal no glia. The stroma is very delicate reticulum bearing blood vessels with only a lining of endothelium and a thin layer of connective tissue cells (Figs. 3 and 4). The arrangement of the cells and their staining reaction suggests a neoplasm of the nerve sheath origin. *Pathologic Diagnosis:* Neurofibrosarcoma of small bowel.

FIG. 3. FIG. 4.

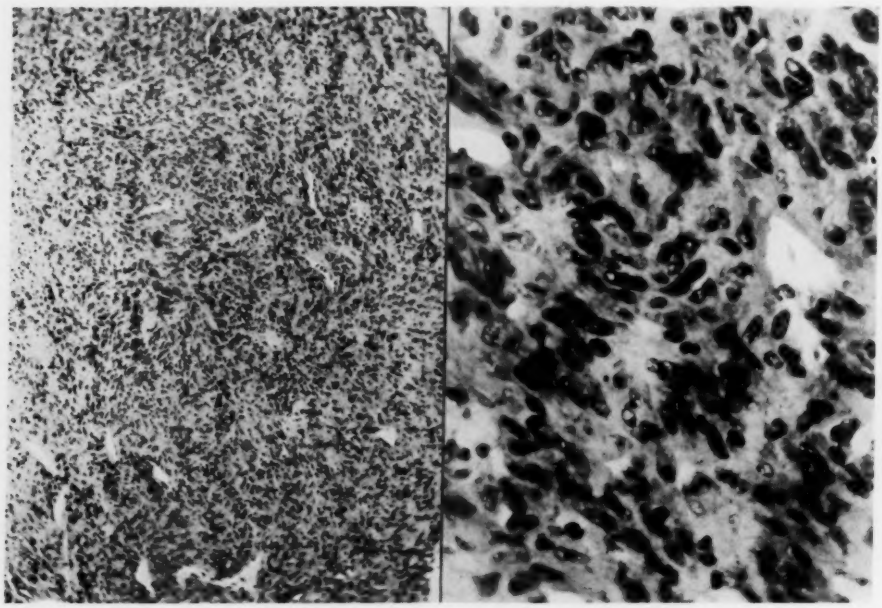

FIG. 3.—Case 1: Photomicrograph showing many bundles of fibers extending in various directions and imperfect palisading. There are numerous blood sinuses. (Low power.)
FIG. 4.—Photomicrograph showing the cells arranged in definite palisades. (High power.)

The patient made an uneventful recovery, temperature never going above 99° F., and she was dismissed from the hospital on the tenth postoperative day, with the advice that she return in four weeks for roentgenotherapy. Six months after operation she was without complaint.

The second case is interesting from the fact that the smaller as well as the larger lesions all present the same picture.

Case 2.—I. B., male, age 47, had consulted a physician on account of loss of weight and was thought to have tuberculosis. He complained only of weakness, loss of weight and vague abdominal discomfort occasionally associated with griping pains.

Physical examination was entirely negative other than for slight tenderness to deep pressure over the left lower quadrant. Roentgenologic examination was negative for tuberculosis. A thorough gastro-intestinal study not only of the stomach and colon, but hourly examinations of the small intestines failed to reveal any abnormalities.

Urinalysis was negative. R.B.C. 3,980,000, hemoglobin 73.3 per cent. W.B.C. 11,150, 77 per cent neutrophils, 14 per cent lymphocytes and 9 per cent monocytes. *Preoperative Diagnosis:* Intra-abdominal malignancy, source unknown.

Operation.—February 15, 1933: Exploration of the abdomen revealed the liver and spleen to be normal. There was no evidence of any carcinoma in the stomach or duodenum. Beneath the ligament of Treitz was a mass about the size of an orange, which had grossly the appearance of ovarian tissue. It was grayish-white in color and extended

up toward the left kidney, but the kidney itself did not appear to be the source of the growth. The right kidney was normal. There were no tumors in any part of the colon. The prostate was apparently normal. No implants of neoplastic tissue were evident in the culdesac. Beginning at the ligament of Treitz and extending throughout the length of the small intestine down to the ileocecal valve were many tumors varying in size. All the lesions except the very largest presented the same characteristics. The largest ones grew outward on the bowel wall, were of a yellow color and apparently were not obstructing the lumen of the intestine. The smallest ones were of a yellowish color, slightly umbilicated, and seemed to spring from the intestine beneath the serosa. In many places, where these tumors were 1 cm. or more in diameter, there was partial intussusception. In none of these was the intussusception of greater length than 2 cm. and all were easily reducible.

It being utterly impossible to remove all of the neoplastic tissue, a resection of approximately 16 inches of the ileum was performed for biopsy purposes.

FIG. 5.—Photograph of section of jejunum with tumors. The ends of the specimen are opened to show the ulceration and the protrusion of the tumors into the bowel lumen causing obstruction.

Pathologic Examination.—Gross: The specimen consists of 38 cm. of the jejunum (Fig. 5). There are five tumor masses in the wall of the bowel, one large one near each end. They are from 0.5 to 4.0 cm. in diameter on the surface and from 0.25 to 2.50 cm. in thickness. All produce some obstruction but the largest one closes the lumen, except for a small opening about 1 cm. in diameter, by protruding into it. They are all covered by serosa, some of them rounded and others puckered and depressed. The mucosa opposite the depressions is ulcerated, but over two of them it is intact. The sectioned surface reveals grayish, very friable neoplastic tissue that is quite vascular and contains numerous small, recent hemorrhages. The margins of the ulcers overhang somewhat, but the lining is not thickened and there is no suggestion of continuity of tumor tissue and mucosa. The margins are infiltrating and the bowel wall destroyed. The main mass of tumor tissue is sometimes internal and sometimes external to the muscle coat.

Microscopically, sections show a neoplasm, made up of a very cellular parenchyma and an inconspicuous, delicate stroma. The cells are arranged in irregular bundles, extending in all directions, and also in imperfect whorls. They are elongated and stellate-shaped with a moderate amount of cytoplasm which is extended into short coarse processes. There is a small amount of fibrillar, intercellular substance. The nuclei are dense with chromatin, but in some cells it is arranged in large granules and there are large nucleoli (Figs. 6 and 7). A few cells show mitosis. Blood vessels are numerous and thin-walled.

The tumor is malignant. Its origin from the nerve sheath is suggested by the

irregular bundles and imperfect whorls of fibers together with the general character of the cells. Whether they are metastatic or multicentric growths cannot be determined with certainty, but since multiple origin is common in this type of neoplasm this interpretation is first choice. *Pathologic Diagnosis:* Neurofibrosarcoma, multiple, of jejunum, with partial obstruction.

Convalescence was uneventful, and the patient was discharged on the fourteenth day postoperative. Death occurred three months later, May 16, 1933. An autopsy was obtained.

Autopsy.—External examination reveals a markedly emaciated white male. The abdomen is moderately distended; in the midline is a well-healed surgical scar. Incision is made in the abdomen only.

FIG. 6.—Photomicrograph showing the tumor invading the submucosa of the ileum. (M) Mucosa. (T) Tumor. The cells are arranged in interlacing bundles and there is imperfect palisading. (Low power.)

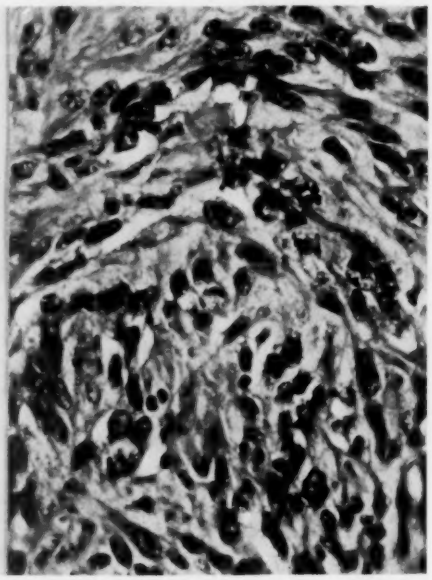

FIG. 7.—Photomicrograph showing two large strands, one curved around the other. Cell outlines are indistinct and morphology moderately irregular. Some cells have coarse fibrils. (High power.)

The peritoneal cavity contains about 1,200 cc. of blood tinged fluid. The thoracic cavities are free from fluid and adhesions. No changes are noted in the gastro-intestinal tract except for the small bowel. It is moderately distended with gas, and the site of the resection is adherent to the parietes anteriorly. At various intervals there are spherical tumors measuring from 1 to 10 cm. in diameter. They are covered by serosa. Some of them are annular with large lumina formed by the necrosis of the inner surfaces (Fig. 8). Many of them form partial obstruction by protrusion into the bowel. Section reveals friable, grayish neoplastic tissue, the central part of which is necrotic, and here and there are old and recent hemorrhages. Some of the inner surfaces are ulcerated, others covered by mucosa. The gross appearance is identical with that of the surgical specimen. In all, 21 tumors are counted in the bowel wall, and there are eight or more in the mesentery and retroperitoneal lymph nodes in the upper half of the abdomen; none are found in the pelvis or at the bifurcation of the aorta. One is found beneath the peritoneum and in front of the left kidney, but the kidney is not invaded.

There are no tumors in the lymph nodes of the thorax or in the viscera of the chest and abdomen, including the adrenals, or in the prostate and testes. There is very early

bronchopneumonia in the posterior aspect of each lung. The liver is small and dark from starvation, and all the viscera are soft from cloudy swelling.

Microscopy reveals a neoplasm identical in structure with that of the surgical specimen, and early bronchopneumonia.

Comment: It does not seem probable that the tumors have arisen from a postperitoneal focus, although a spread by way of the superior mesenteric artery would explain their location except for the one anterior to the kidney, and if this had happened the colon could have received metastases. The location of some of the masses will admit the possibility of a primary focus in one of the semilunar ganglia or others of

FIG. 8.—Photograph of the distal two-thirds of the small bowel and part of its mesentery. There are numerous enlargements caused by tumor growth in the wall. The largest one (T) is a truncated tumor replacing the bowel with a lumen through it. There are also masses in the mesentery.

the sympathetics and, if so, the ganglion was completely destroyed. The largest tumors are in the bowel wall, however, and phosphotungstic acid stains reveal no glia fibers. Nerve sheath tumors are commonly multicentric, although there are no definite criteria by which it can be determined which of these tumors arose by metastasis or by neoplasia.

Postmortem Findings.—Neurofibrosarcoma of small intestine; metastasis to mesenteric and postperitoneal lymph nodes; other postperitoneal metastases; emaciation; early bronchopneumonia.

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DILATATION OF THE COLON*

REPORT OF A CASE FOLLOWING THE DEVELOPMENT OF AN AORTIC ANEURYSM; RELIEVED BY DILATATION OF THE ANAL SPHINCTERS

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MEGACOLON, or better termed dilatation of the colon, may be classified into two types: Congenital or idiopathic; and acquired or secondary. The former is not caused by any organic obstruction and is present at birth or evidenced by signs and symptoms in early childhood. The latter may appear in childhood, but occurs more commonly later in life, and is secondary to a gradually increasing partial obstruction of the rectum or sigmoid. The cases of the idiopathic type, when first recognized in late childhood or later in life, can be traced back to early childhood, by a long history of a distended abdomen and obstipation, characterized by bowel movements at intervals which may vary from three days to several weeks.

Case Report.—Hosp. No. 96215: F. V., white, male, age 73, was admitted to the Medical Service, St. Luke's Hospital, New York, August 3, 1937, complaining of increasing swelling of the abdomen during the preceding two months, associated with obstipation which had become so complete that he had had no bowel movement for several days preceding his admission. During the two months of his present illness he had lost 20 pounds in weight. In addition to the acute condition, he gave a history of having had a moderate degree of constipation for many years, but one which had been in no way remarkable, having been readily controlled by the use of mineral oil and enemata.

In 1932, at the age of 68, he had been operated upon at St. Luke's Hospital, for an acutely thrombosed hemorrhoid, which was excised, with complete relief. At that time, his physical examination was otherwise negative, and the abdomen was described as being flat and flabby, without distention. In 1935, he returned to the Medical Clinic because of fatigue. Slight widening of the aortic arch and moderate enlargement of the heart were found. The abdomen was described as entirely negative. The blood Wassermann reaction was negative. At intervals during the next two years, he was seen in the Medical Clinic and treated as a cardiac case. A gradual increase in the width of the aorta was noted; eventually, a definite aneurysm of the descending aorta presented. The abdomen was not found distended at any of the examinations in the clinic.

Physical Examination.—The patient appeared chronically ill. Percussion revealed an aneurysm of the aortic arch and the descending aorta (Fig. 1). At both bases were a few moist râles. The abdomen was enormously distended, tense and tympanitic. Rectal examination was negative except that the sphincter was about the size and shape of a closed fist. It was very tense and spastic, but there was no stricture in the muscle or the areas about it, only a condition of firm contraction in a greatly hypertrophied sphincter. Proctoscopic and sigmoidoscopic examinations were negative.

Neurologic examination revealed the deep reflexes absent throughout with the excep-

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tion of the left knee jerk, which was obtained with reinforcement. The abdominal reflex on the left was greater than the right. Vibratory sensation was decreased in the feet. The gait was unsteady with the eyes closed. The fundi showed marked arteriosclerosis. The pupils were unequal and small but reacted to light and accommodation. *Neurologic Diagnosis:* Subacute combined sclerosis, arteriosclerotic degeneration of the cord.

An electrocardiogram, August 4, 1937, showed normal rhythm, left preponderance, inverted T-wave in Lead I—evidence of myocardial damage. Another, on August 18, was the same with the exception that Lead II also presented an inverted T-wave.

When roentgenograms were made following barium installation into the colon, the

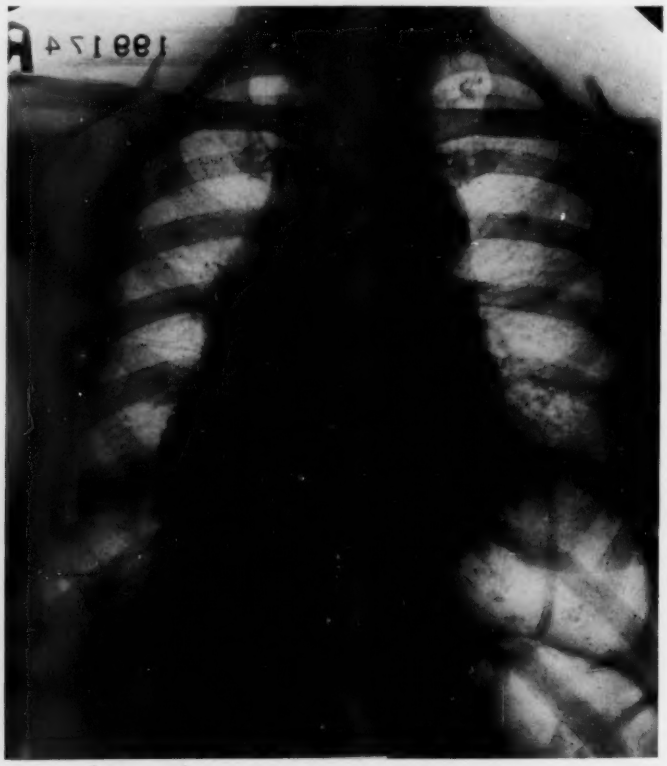

FIG. 1.—Roentgenogram of the chest made on July 30, 1937. The aneurysm of the aortic arch and the descending aorta can be seen. The trachea is deviated to the right. There is moderate enlargement of the heart. The distended colon can be seen pushing both sides of the diaphragm upward.

abdomen was found to be so enormous that it was necessary to film it in sections (Figs. 2, 3 and 4). The barium could be forced only into the transverse colon because of the size of the large intestine and the large amount of gas and fluid which it contained. The clysma revealed an enormous dilatation of the entire large bowel. Those portions not outlined by barium were readily seen due to their distention with gas.

A regimen of enemata and colon irrigations gave practically no relief. Because of the patient's poor physical condition, resection of the presacral nerve was considered to be contraindicated.

Procedure.—August 25, 1937 (after three weeks of unsuccessful medical treatment): Under gas-oxygen anesthesia, the anal sphincters were slowly dilated until the whole hand could be introduced into the rectum. For several days following this treatment there

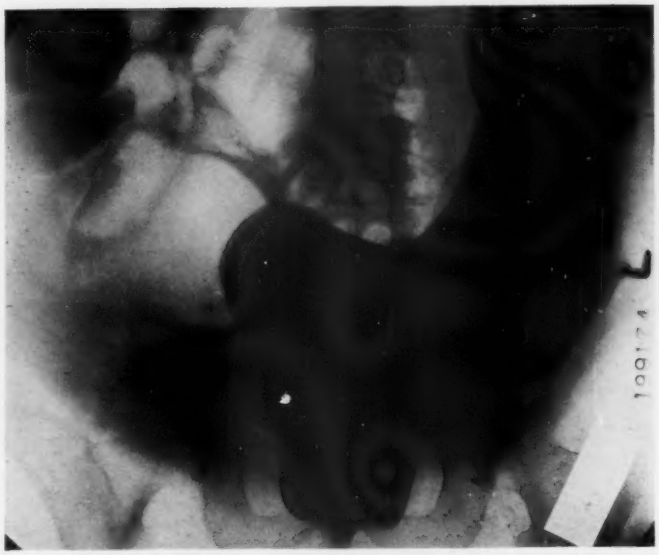

FIG. 2.—Roentgenogram of a clysma taken on August 4, 1937. The rectum, sigmoid and lower part of the descending colon can be seen to contain barium. The outline of the cecum, part of the ascending colon, and a loop of the transverse colon are shown outlined by their contained gas.

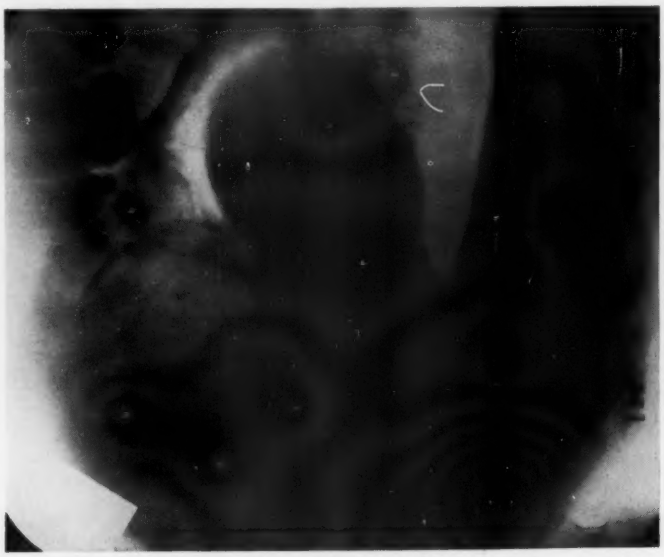

FIG. 3.—Roentgenogram taken somewhat higher than that shown in Fig. 2, and after more barium had been allowed to run into the colon. The size of the sigmoid is better shown. Some barium has now reached the ascending colon although the cecum contains only gas and non-opaque fluid.

was nearly complete rectal incontinence, which then gradually disappeared. He was given daily colon irrigations with excellent results. Large quantities of liquid feces passed from the rectum almost continuously. His abdomen rapidly became smaller.

On September 3, 1937 (nine days after the dilatation), the abdomen had returned to normal size, a reduction of 19 inches in diameter. The bowel movements were under good control. Palpation of the abdomen, now that it was deflated, revealed no aneurysm of the abdominal aorta or other masses. A barium clysma showed the large bowel greatly diminished in diameter (Fig. 5). He was discharged September 8, 1937; symptomatically, completely cured and with the contour of his abdomen normal.

Eight months after discharge, his physical condition had become markedly improved and he had gained about 15 pounds in weight. His blood Wassermann reaction was again negative. Blood count: Hb. 72 per cent, R.B.C. 4,100,000, W.B.C. 7,200, polymorphonuclears 70 per cent, lymphocytes 23 per cent, mononuclears 1 per cent, eosinophils 5 per cent and basophils 1 per cent. The neurologic examination was unchanged.

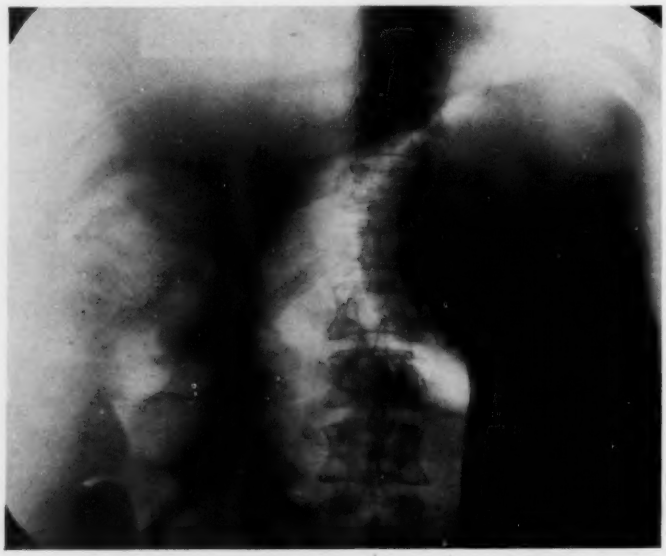

FIG. 4.—Roentgenogram of the upper part of the abdomen. The barium has reached the splenic flexure. There is also a small amount in the ascending colon. The distended loops of the transverse colon can also be seen. Note that in the three roentgenograms of the clysma the lateral extent of the ascending and descending colon is beyond the edges of the films which are 16½ inches wide.

When last seen, nine months after the dilatation, the bowel movements were well controlled by the use of mineral oil, dietary regimen and enemata. The contour of the abdomen had remained normal. He had maintained his gain in weight and his general physical condition was somewhat improved.

Discussion.—After a brief search of the literature, no reference could be found of dilatation of the colon following the development of an aortic aneurysm or associated with a subacute combined sclerosis, nor was any reference found to the procedure of dilatation of the anal sphincters as a treatment for the idiopathic type of dilatation of the colon. Two articles[1, 2] did, however, report six cases successfully treated by partial sphincterectomy. At present, children with idiopathic dilatation of the colon are being treated,

apparently successfully, by the use of syntropan and, thereby, avoiding resection of the presacral nerve.

The case which is reported herewith is unique in a number of respects. Insofar as it is possible to tell, the dilatation of the colon was not congenital, nor was it caused by any organic obstruction, as is ordinarily the case when this condition is of the acquired type. It appeared late in life (age 73)

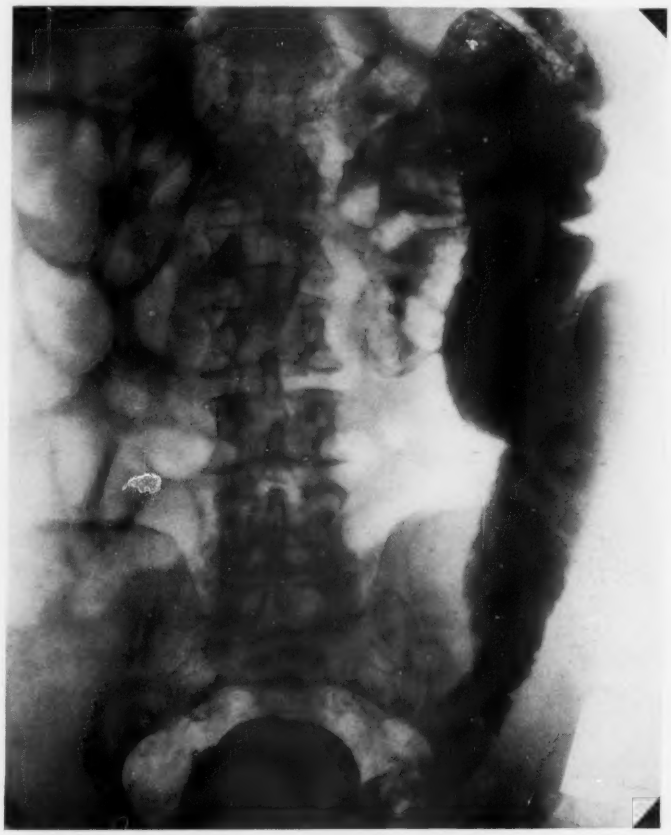

FIG. 5.—Roentgenogram of a clysma taken on September 3, 1937, which was 9 days after the dilatation of the sphincters. The decrease in the size of the colon is readily noted. The barium has reached the distal part of the transverse colon. The more proximal portions of the colon are seen to contain gas but are less in diameter than in the roentgenograms made before the dilatation. The abdomen had decreased 19 inches in diameter in the interval.

following the development of an aortic aneurysm and a subacute combined sclerosis due to arteriosclerotic degeneration of the cord. Whether or not either of these conditions was an etiologic factor, by causing an imbalance of nerve impulses to the sphincters and possibly to the colon, one cannot say. This possibility must, however, be considered.

The result obtained by thorough dilatation of the anal sphincters was much better than had been hoped for at the time it was employed as a form of treatment in this case, in that the relief obtained was complete and to

date (after a period of over nine months) that relief has continued. Of course, only time will tell whether or not this relief will be permanent. The expectation is that in all probability it will be only temporary. However, he will stand successive dilatations, should the necessity arise, much better than an extirpation of the presacral nerve.

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CELIAC GANGLIONECTOMY AND PLEXUS RESECTION FOR TABETIC GASTRIC CRISES

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TABETIC gastric crises which do not react to conservative medical treatment have stimulated the performance of a variety of surgical procedures, with indifferent results. The author desires to report a case of gastric crises satisfactorily treated by excision of the celiac ganglia and plexus and periarterial sympathectomy of the celiac axis and branches, following successful preoperative diagnostic novocain block.

The typical gastric crisis is characterized by severe abdominal pain and vomiting. It is generally understood that pain originating in the stomach travels over sympathetic pathways to the celiac plexus and ganglia and then, solely, over the splanchnic nerves. Vomiting is a reflex reaction. The afferent component may be mediated through vagal fibers in the stomach, sensory nerves, or other afferent nerves; irrespective of their origin, they reach the medulla. The efferent impulses producing tonic contraction of the pylorus and antrum are transmitted over the vagus; those inhibiting the fundus and relaxing the cardia are transmitted over the splanchnic nerves.

The celiac plexus and ganglia have important anatomic connections with the vagi. Gastric fibers of vagal origin travel into and through these structures, some coursing, in company with sympathetic fibers, in the left gastric, splenic, and hepatic periarterial plexuses. Splanchnicectomy alone would not affect these vagal fibers, whereas extirpation of the celiac ganglia and plexus, and periarterial sympathectomy of the branches of the celiac axis would have the obvious advantage of a combined sympathetic and vagal interruption. The author knows of no previous case in which this method of treatment has been employed for the control of tabetic gastric crisis.

Case Report.—Service of Dr. Harold Brunn: S. J., male, age 46, complained of severe gastric crises of tabetic origin. He had a constant burning sensation over the xiphoid. At the onset of a crisis this burning became aggravated after a meal, changed to a sharp pain and radiated to the back. This was followed by nausea and finally vomiting with marked retching. On several occasions he vomited blood. Since their onset, in 1913, these crises had occurred in rapid succession, with intervals of respite between attacks of only one or two days, except for a period of three weeks in 1919. During the past few years they have become more severe and of longer duration, lasting, at times, as long as ten days, and consisting of constant pain and vomiting. In the interval between attacks, belching was a frequent and annoying symptom.

At the age of 16, he had a penile lesion without secondaries. In 1913, his blood Wassermann was found to be 2+. He had urinary retention. Antiluetic treatment was instituted and since then his blood Wassermann and Kahn have been negative on five

Submitted for publication March 8, 1938.

occasions and his spinal fluid has been normal on three occasions, the last time in October, 1936. He had vigorous antiluetic therapy since 1919, when the diagnosis of tabes was first made. He had three pyrotherapy treatments in 1924. The following objective findings substantiated the diagnosis: (1) Pupils asymmetrical, reaction to light markedly impaired on both sides, especially on the right; reaction to accommodation impaired; (2) slight atrophy of both optic disks; (3) absent patellar and Achilles reflexes; (4) Romberg positive; (5) bands of disturbed sensation in the lower dorsal and lumbar distribution; and (6) bladder retention. Drs. Leroy Briggs and M. R. Hirschfield concurred in the diagnosis of tabes dorsalis. Gastro-intestinal roentgenograms were negative on three occasions.

During the entire course of his illness the picture was obscured by a marked radiculitis involving the roots from the sixth dorsal to the fourth lumbar but most often from the tenth dorsal to the fourth lumbar with varying anesthesia, hypesthesia, hyperesthesia, and paresthesia in the areas of distribution. In addition, there were complicating symptoms of a widespread hypertrophic arthritis of the thoracic spine. In May, 1935, 1 cc. of absolute alcohol was injected into the lumbar subarachnoid space in the hope of relieving lightning pains in the lower extremities, with a satisfactory result. In April, 1936, he was fitted with a brace which immobilized his thoracic spine with considerable relief.

Despite all efforts the crises progressed. The patient was seen by the author, June 9, 1935, during an unusually severe crisis which had already persisted for three days. He had only slight and transient relief from two hypodermics of morphine sulfate, and was in a state of collapse. The region in front of the first and second lumbar vertebrae was then suffused with 20 cc. of 1 per cent novocain injected on each side according to the method of Labat for splanchnic block. In 15 minutes there was a spectacular relief of both pain and vomiting.

In view of the failure of medical management, the increasing severity and duration of the crises, and encouraged by the successful result of diagnostic novocain block of the celiac plexus and ganglia, surgical removal of these structures was offered to the patient with no guarantee as to the result. Before operation, tests were made to act as a basis of comparison for any possible effect of the operation on organs supplied by the celiac plexus and ganglia.

Operation.—October 10, 1936: The abdomen was opened through a left upper paramedian incision. There was no evidence of organic disease of the stomach, duodenum, kidneys, pancreas, liver, or small intestine. The stomach was drawn caudad and a vertical rent made in the gastrohepatic omentum directly in the midline. The pancreas was drawn gently caudad, exposing the celiac axis. The celiac plexus was excised as completely as possible. The anterior surface of the aorta was denuded of sympathetic fibers in this region. It was, of course, impossible to resect all the sympathetic fibers in this area. The dissection was made unusually difficult by the presence of a number of large veins and venous plexuses. A periarterial sympathectomy was then performed on the celiac axis and its branches. The left gastric artery was cut between ligatures of silk. The splenic artery was denuded of all its adventitia for a distance of one inch from its origin. In the dissection it was injured and was ligated. The hepatic artery was successfully denuded for a distance of one inch from its origin. There was a heavy layer of interlacing sympathetic fibers on these vessels. After the adventitia had been removed, the diameter of the artery was reduced almost one-half. The splanchnic nerves were then cut close to their attachments to the celiac and aorticorenal ganglia. The suprarenal glands were exposed separately, and the wide band of fibers connecting the celiac ganglia and plexus to the suprarenal glands was sectioned on each side close to the suprarenal glands. The celiac and aorticorenal ganglia were then removed. The rent in the gastrohepatic omentum was approximated and the abdominal cavity closed in layers. The postoperative course was uneventful.

Subsequent Course.—Since operation there has been a great improvement in his gastric symptoms. He had only six very mild and short attacks of nausea and vomiting.

These occurred following unusually severe root pains in the legs and groin, or psychic upsets. Except for these attacks, he has been free of gastric symptoms, and the improvement has persisted until the present, 26 months after operation. He has a good appetite and eats and drinks everything, including alcohol and the foods he previously could not tolerate.

TABLE I

LABORATORY DATA

	Preoperative	2 Wks. Postoper.	3½ Mos. Postoper.	Almost 1 Yr. Postoper.
Blood Chemistry				
Amylase	4 units	3	4.6	7.5
N.P.N.	34 mg. per 100 cc.	25	28.3	27.3
Cholesterol	178 mg. per 100 cc.	190	157	178.5
Chlorides	445 mg. per 100 cc.	495	448	420

Glucose Tolerance Tests

	Blood Sugar	Urine Sugar	Blood Sugar	Urine Sugar	Blood Sugar	Urine Sugar	Blood Sugar	Urine Sugar
Fasting	60 mg. per 100 cc.	0	65	0	62	0	64.5	0
½ hr.	111 mg. per 100 cc.	0	142	0	181	0	100.0	—
1 hr.	121 mg. per 100 cc.	0	133	0	167	0	142.8	—
2 hrs.	80 mg. per 100 cc.	0	60	0	64	0	62.0	0

Gastric Analyses

	Fast	1	2	3	Fast	1	2	3	Fast	1	2	3	Fast	1	2	3
Volume	9	5	4	7	14	10	5	12	13	12	16	29				
Mucus	x	x	x	x	x	x	x	x	x	x	x	x				
Free HCl	14	6	7	13	30	7	20	32	11	8	16	38	20	8	12	11
Total HCl	25	14	15	34	46	11	40	40	39	26	34	48	50	34	38	26
Bile Pig	0	0	0	0	x	x	x	x	x	x	x	x	0	0	0	0
Blood (occult)					x	x	x	x	x	x	x	x				
Blood (gross)					0	0	0	0	0	0	0	x				

Kidney Function Studies

Intramuscular Phenosulphonphthalein			
1st hr.	40%	35%	5%
2nd hr.	5%	30%	15%
Addis' conc. count	Within normal limits	Within normal limits	

Laboratory studies were made before operation and on three occasions after operation (Table I). There was no evidence of significant postoperative change in the blood nonprotein nitrogen, amylase, cholesterol, chlorides, or sugar; no abnormal variation in glucose tolerance test, phenolsulphonphthalein excretion test, Addis' kidney concentration test, or uranalysis; and normal levels in gastric free and total acidity. Likewise, Brown[2]

found no demonstrable changes in the gastric acidity of three cats treated by bilateral celiac ganglionectomy. The tests did not confirm in humans the increased glucose tolerance reported by DeTakats and Cuthbert[3] in dogs similarly treated. The clinical course gave no evidence of disturbed function of the kidneys, pancreas, or stomach. Before operation his blood pressure varied between 130/80 and 140/80; after operation between 100/66 and 140/90.

These results are not indicative of the effect of such an operation in cases of diabetes or hypertension. The operation is one directed toward alteration of function, and the results upon normally functioning organs are not the gauge of its possible effect on dysfunctioning organs. One may conclude that removal of the human celiac ganglia and plexus is not followed by any disturbance of function in organs supplied by it, insofar as one is able to judge by the tests reported herein or in the clinical course of the patient.

SUMMARY AND CONCLUSIONS

A case is reported of intractable gastric crises of tabetic origin relieved following surgical excision of the celiac plexus and ganglia. The site of surgical attack was determined by a successful preoperative diagnostic novocain block of the region in front of the first and second lumbar vertebrae. The improvement has persisted until date, 26 months after operation. Preoperative and postoperative laboratory studies show no significant changes in the function of the stomach, pancreas, or kidneys, and no abnormal alteration of blood chemistry. The operation had no apparent ill effects, as indicated by laboratory studies or clinical course.

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BILATERAL AND UNILATERAL RENAL AGENESIS

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CONGENITAL abnormalities of the upper urinary tract have been reported much more frequently in recent years due to the increased interest and investigations of both the urologist and pathologist. We are concerned here with the postmortem findings of 12 cases of renal anomalies of which two were bilateral absence of kidneys, and ten were congenital solitary kidneys.

Bilateral Renal Agenesis.—Bilateral metanephric agenesia is a rare anomaly, and is a condition incompatible with extra-uterine life. The fetus is frequently alive at birth, but death occurs in a few hours. This condition is usually associated with other equally serious defects of development. In a very thorough review of the literature, Amolsch[1] reported 119 cases, including four of his own, which with the two cases herewith reported, totals 121 cases of bilateral renal agenesia. These were the only two instances of complete absence of both kidneys found in over 12,000 autopsies performed at Cook County Hospital since 1929.

CASE REPORTS

Case 1.—Anna B. was born at full term and lived 18 minutes.

Postmortem Examination revealed a cyanotic, white female infant, weighing two and one-half pounds, and measuring 33 cm. total length with umbilical cord attached. The head is much flattened from side-to-side; and blood exudes from the nose. No mention was made of the internal organs. The kidneys, ureters, and renal arteries cannot be found. The external genitalia are normal appearing. The opening of the urethra is wide, and located 1 cm. from the region of the clitoris. It is normal and located on the anterior vaginal wall. Its circumference is 7 Mm., and it leads into a much narrowed tube-like bladder which is 25 Mm. long and 3 Mm. in diameter. From the upper end of the bladder, an obliterated cord-like urachus, 17 Mm. long and 2 Mm. in diameter, extends up to the umbilicus and is accompanied by the umbilical arteries which are patent. No ureteral openings (orifices) can be found in the bladder. Beyond the urethral opening, the vagina extends only as a small pocket 1 Mm. in diameter and 3 Mm. long. No uterus, fallopian tubes or ovaries can be definitely made out, and no culdesac is present. Lying on the serosa of the posterior lumbar muscles on both sides there are elongated, light pinkish-yellow structures. The left one is 30x3x1 Mm. The right is 32x2x1 Mm. From the lower ends very fine cord-like structures extend downward. On the left side this structure ends behind the upper end of the bladder. On the right side it seems to disappear into the fascia along the external iliac artery.

Microscopically, the flat bodies in the lumbar region are found to be ovaries, in which numerous well developed primordial follicles are present and imbedded in a cellular stroma with ill defined cords of cuboidal cells. The cords extending from these bodies to the bladder consist only of connective and fat tissue and blood vessels. A transverse section taken through the bladder and rectum in the region normally occupied by the uterus shows bladder and rectum connected by loose vascular connective tissue in which there is

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no indication of a uterine anlage. The same holds true of a vertical section made through this region. The adrenals were not recorded.

Case 2.—Paul M. was born at seven and one-half months, and lived three hours.

Postmortem Examination revealed a white, male infant, weighing 2,060 Gm. that measured 40 cm. total length. The essential findings were the absence of both kidneys and ureters; the renal arteries were very narrow as was also the right renal vein; the bladder was small and contracted; ureteral orifices were not found; penis and testes were normal. The adrenals were not recorded.

Etiology.—No single factor can fully explain all recorded cases of renal agenesia. They are always accompanied by some evidence of maldevelopment in distant and not closely related organs. The most popular etiologic concept is that of abnormal pressure exerted during embryonic development by inflammation, or by decrease or absence of amniotic fluid, or by amniotic adhesions. It is true that in some cases pressure by any of the above factors on the caudal myotomes may stunt the growth of the caudal end of the wolffian duct and result in renal agenesis. But this is true of only a small percentage of cases. Rainer[2] believes that the differentiation of the nephrogenic cap is dependent upon the stimulus evoked by the growth of the ureteral bud into the nephrogenic cord. This view is supported by the fact that no instances are recorded of a formed metanephros in the absence of a ureteral bud. Instances are recorded in which ureteral structures were developed, but no metanephros.

A tenable explanation of bilateral renal agenesis has been offered on the basis of germ plasm defects. Support for this assumption is made in the report of Madisson[3] of two cases of bilateral renal agenesia (not in twins) occurring in fetuses born of the same mother. It is probable that the germ plasm may be deficient in the ability to produce a normal metanephros.

The consummation of the renal system depends upon the formation of the ureteral bud and its subsequent penetration into the nephrogenic mesenchyme. The etiology of bilateral renal agenesis rests on three possible errors of development: The ureteral bud may fail to appear; it may appear, but fail to reach the nephrogenic tissue; or the nephrogenic cap may fail to develop.

Congenital Solitary Kidney.—Congenital solitary kidney, or unilateral renal agenesis, is a condition brought about by a more or less complete lack of unilateral development of the upper urinary tract, and is much more common than bilateral renal agenesis. As the result of improved diagnostic methods and increased clinical reports, congenital solitary kidney is more frequently diagnosed, especially since the wide use of intravenous urography. In a true case of congenital solitary kidney, no tissue is found on one side that can be identified microscopically as renal parenchyma.

It must be differentiated from the fused kidney, the aplastic kidney, the hypoplastic kidney, as well as from atrophy of the kidney. Gutierrez[4] has classified these different types of undeveloped kidney, and believes that from 35 to 40 per cent of the cases reported as congenital absence of one kidney are not authentic cases. Renal aplasia is considered to be four times more common than unilateral renal agenesis. There are two groups of true solitary

kidney. In one group, there is a complete absence of both the kidney and the ureter on one side, the single kidney may be ectopic or cross ectopic, but there is only one ureteral orifice opening in the bladder, and half of the trigone has not developed. This anomaly is usually accompanied by some form of congenital malformation, particularly of the genital tract. The other group consists of that type of solitary fused kidney in which there is evidence of union of two nephroblastemata into one organ which has two pelves and two corresponding ureters, opening normally or abnormally into the bladder.

Autopsy records from various reports indicate that unilateral renal agenesis is found once in about 1,000 postmortems. Ten were found in 12,000 autopsies at Cook County Hospital, and ten were found in 13,000 autopsies at Bellevue Hospital (Campbell[5]). Many cases of congenital absence of one kidney have been reported, and the literature has been reviewed by Ballowitz[6] (1895), Moore[7] (1898), Radasch[8] (1908), Anders[9] (1910), Dorland[10] (1911), Eisendrath[11] (1923), Goldstein[12] (1925), and Hennessey[13] (1929). More recently, Collins,[14] in 1932, reviewed the study of 581 cases of congenital unilateral renal agenesis, among which were included nine cases from the Mayo Clinic, found in a series of 6,349 consecutive postmortem examinations. He found the incidence of congenital solitary kidney to be 367 in 337,488 autopsies, and one in 920 postmortems. Males were more frequently affected (281 to 231); the right kidney is more often absent (238 to 218); and the average age is over 20.

Eisendrath and Rolnick[15] mention the following combinations of congenital solitary kidney:

(1) Complete absence of kidney, ureter and ureteral orifice on one side: This type is the most common, and was present in eight of our cases. Hennessey found it present in 273 of 350 cases, and it occurred in over 400 of 581 cases reviewed by Collins. It is this type that is also accompanied by other congenital malformations, especially of female genital organs. The corresponding half of the trigone was reported as being absent in 44 cases (Collins).

(2) Complete absence of kidney, ureter and ureteral orifice, but the ureter ends at the opposite side of bladder (solitary crossed kidney): They collected four such cases from the literature, and recently, Beer and Ferber[16] reported a similar case.

(3) Kidney alone absent: Rudimentary ureter, usually short ends in normally placed and developed ureteral orifice. This type, with a normal looking ureteral orifice and a ureter of variable length, may be overlooked cystoscopically. It was found in two of our cases: in one, the ureter was about 8 cm. long, and in the other, 1 cm. long, both ending in a blind pouch. The ureter, varying in extent from a short blind pouch to one of normal length, was found in over 10 per cent of the series reported by Hennessey.

(4) Complete absence of kidney, ureter, and vesical orifice on one side. Opposite kidney, ectopic or pelvic, and the ureter may end in the midline of bladder. Eisendrath reported seven, and Hennessey collected two such cases. Recently, Stevens[17] reviewed the literature and found 27 cases of pelvic

solitary kidney which included two of his own cases. He stated that true pelvic solitary kidney makes up 4 or 5 per cent of unilateral renal agenesis, and that we may expect to find one case in every 22,000 persons.

Embryology.—The complete absence of one kidney is best explained by the failure of the ureteral bud to develop. It is not caused by the absence of the metanephric blastema (Hinman[18]). It may be due to early degeneration of the ureteral bud, but this can be proven only when some remnant of the kidney remains. Fortune[19] has proposed four theories as the cause of the condition:

(1) The metanephric bud may fail to appear in spite of a normal preceding mesonephros.

(2) The metanephros may appear, but undergo early degeneration.

(3) The mesonephros may be imperfectly developed.

(4) The pronephros may fail to develop, and, therefore, the mesonephros does not grow.

The marked frequency with which genital anomalies are found in these cases of unilateral renal agenesis is due to the fact that the corresponding müllerian duct on the agenetic side is absent, and this embryonic defect is responsible for the absence of the genital organs so strikingly seen in females. The müllerian duct develops later than the wolffian duct, and the chance for malformation is greater. Genital anomalies were found in three of the ten cases herein reviewed. Hennessey found genital anomalies in one-third of his series, and Collins recorded the presence of malformations of the genital tract in 338 of 581 cases of congenital solitary kidney, 129 being in males, and 209 in females. It is interesting to note that Stevens found genital anomalies in 13 of the 27 cases found, all in females, and in eight cases no mention of genital defect was made by the different writers.

Mention must be made of the significant fact that the adrenal gland has been found to be absent in a certain percentage of cases of unilateral renal agenesis. The cortical portion of the adrenal is derived from the columns of cells which bud off from the wolffian body, and is of mesoblastic origin; while the medullary portion of the gland is developed in connection with the sympathetic nervous system, and is mainly of epiblastic origin. Since the nephrogenic tissues of the wolffian duct are absent and have not developed the kidney, it may be assumed that the adrenal, lacking one of its essential elements, is also absent. Gutierrez suggests a new theory, that when a kidney is not formed, the adrenal on the corresponding side is not formed, and offers this as a differential point of renal agenesis from renal aplasia or hypoplastic kidney, as in the last two conditions the adrenal is invariably present. The adrenal was absent in two of our cases, and not mentioned in eight. Collins stated that it was absent in 66, atrophic in four, normal in 129, hypertrophic in 13, and not stated in 369 cases of the 581 reported. He also states that "the suprarenal glands are not intimately connected with this development (metanephros), and hence are rarely absent even if the kidney or the other related unilateral structures are absent." Eisendrath believes that the adrenal is

TABLE I

ANALYSIS OF POSTMORTEM FINDINGS IN TEN CASES OF CONGENITAL SOLITARY KIDNEY

Case	Age	Sex	Side	Adrenals	Ureter	Bladder	Genitalia	Principal Disease	Kidney
1. L. M.	40 yrs.	F.	R.	Not recorded	Absent	No orifice	Normal	Huge cyst of ovary, compressing left ureter	Hydronephrosis. Hydro-ureter
2. H. S.	40 yrs.	F.	R.	Not recorded	8 cm. long, ending in blind pouch	Dimple	Normal	Carcinoma of breast	Normal
3. M. H.	38 yrs.	F.	L.	Absent	Absent	No orifice	Hypoplastic left tube and ovary	Uremia	Glomerulonephritis
4. A. D.	1 mo.	M.	L.	Not recorded	Absent	No orifice	Absent left vas deferens, testicle, and seminal vesicle	Uremia	Fetal lobulations of right kidney with marked dilated calices and ureter
5. J. A.	10 mos.	M.	L.	Not recorded	Absent	No orifice	Normal	Bronchopneumonia	Hydronephrosis, due to aberrant vessel
6. B. M.	15 mos.	M.	R.	Not recorded	1 cm. long, ending in blind pouch	Dimple	Normal. Harelip, cleft palate	Bronchopneumonia	Hyperplasia
7. B. J.	7 hrs.	M.	R.	Not recorded	Absent	No orifice	Undescended testicles Hypospadius	Congenital. Pulmonary atelectasis	Normal
8. M. W.	56 yrs.	M.	L.	Not recorded	Absent	No orifice	Normal	Coronary thrombosis	Hyperplasia
9. L. A.	20 yrs.	F.	R.	Absent	Absent	No orifice	Normal	Uremia	Glomerulonephritis
10. M. C.	21 yrs.	F.	L.	Not recorded	Absent	No orifice	Normal	Uremia	Glomerulonephritis

present in 75 per cent of cases of unilateral renal agenesis. Amolsch found that the suprarenals were rarely affected in bilateral renal agenesis since they were bilaterally absent only twice and unilaterally absent four times in 119 cases. It is difficult to explain this marked difference of opinion in regard to the relationship of the presence or absence of the adrenals in cases of renal agenesis.

The clinical importance of solitary kidney is evidenced in renal surgery, as the literature contains cases of anuria and death following nephrectomy in such cases, as the result of errors in diagnoses. The diagnoses of congenital solitary kidney will never be missed if ureteral catheters are employed in every instance and a check-up is made by excretory urography. The solitary single kidney is anatomically and physiologically enlarged, owing mainly to the compensatory functional hypertrophy. It is of great importance to note that a congenital solitary kidney is not a serious menace to life unless a genito-urinary tract disease is present, and then a much poorer, if not fatal, prognosis is offered. Sixty-eight point three per cent of the patients in Collins' report expired from diseases totally unrelated to the genito-urinary system. In this series, a marked hydronephrosis was found in Cases 1 and 5, and glomerulonephritis was present in Cases 3, 9 and 10. Among the diseases of the kidney mentioned as the cause of death, in order of frequency, are renal and ureteral calculus, pyelonephritis and pyonephritis, chronic nephritis, hydronephrosis, renal tuberculosis, and stricture of the ureter.

Conservative measures are usually employed to treat obstructive and infective conditions of a congenital solitary kidney, but in cases of impending uremic symptoms, as in renal or ureteral calculi (anuria), or pyelonephritis or pyonephrosis, surgery must be resorted to immediately. A pyelotomy or nephrostomy, to establish drainage, has often been a life-saving procedure.

SUMMARY

(1) Twelve cases of renal anomalies found at postmortem are reported.

(2) Two cases of bilateral renal agenesis are recorded, making the total number of cases reported 121.

(3) Bilateral renal agenesis occurs in about one out of 6,000 autopsies.

(4) Ten cases of congenital solitary kidney are recorded in which the kidney, ureter and ureteral orifice were absent in eight cases, rudimentary ureters were present in two cases, associated genital anomalies were found in three, and the adrenal gland was absent in two and not recorded in eight cases.

(5) Bilateral renal agenesis is usually found at autopsy, but unilateral renal agenesis is diagnosed more frequently, and proper treatment instituted much earlier than previously, as the result of improved diagnostic methods and a more general employment of intravenous urography.

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DERMOID CYST OF THE BLADDER

CASE REPORT

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DERMOID cysts of the bladder are extremely rare. The number of cases thus far published does not exceed 15. They may exhibit symptoms of cystitis and offer as a pathognomonic sign, the discharging of hairs on urination (pilimictio). They may occur as a tumor protruding into the bladder cavity, or as a paravesical cyst, which invades the bladder and communicates with it through a small channel, as was the case in the present instance. The treatment consists in the removal of the cyst, either by an intra- or extravesical procedure, or by a combined approach. In the case herewith reported, the dilating of the communicating fistulous tract and the removal of the contents of the cyst caused its reduction to the size of a small diverticulum and to a subsidence of the pathologic process in the bladder; followed by clinical recovery.

Case Report.—B. M., white, female, age 30, single, nullipara, was admitted to the University Clinic February 1, 1938, complaining of frequency, pain on urination and the passage of fetid, turbid urine. The present illness had begun four months previously. She had remained in bed for two weeks before consulting a doctor. During the ensuing three and one-half months, all local and medicinal measures proved ineffectual and the frequency and dysuria had increased. Her family and previous history were irrelevant.

Physical Examination.—The patient was well proportioned but poorly nourished. Temperature 39° C., pulse 125. Palpation of the suprapubic region was painful. Examination of the chest and abdomen was negative. W.B.C. 8,100. Urine: Turbid, alkaline, fetid, sp. gr. 1.015.; the sediment contained red and white blood cells and ammonium-magnesium phosphate crystals. Cystoscopy could not be performed because of the small capacity of the bladder and the intolerance of the patient, who ejected all fluids introduced intravesically. It was noted, however, that the cystoscope met with a definite resistance. *Roentgenologic Examination* showed a dense mesial shadow behind the pubes and another smaller one, of irregular density, partially superimposed upon the right upper aspect of the denser shadow (Fig. 1). A cystogram showed that the first shadow did not alter while the second became considerably larger and its contour more definite (Fig. 2). *Preoperative Diagnosis:* Calculosis vesicae.

Operation.—Under local anesthesia, a suprapubic incision disclosed a hard, yellow stone, the size of a walnut, weighing 12 Gm. This was extracted from the bladder. Looking further for the source of the other shadow on the roentgenogram, the forefinger encountered an opening about ¼ cm. in diameter to the right of the internal orifice of the urethra. The opening was dilated with the forefinger to a diameter of 1.5x1.5 cm., and enabled the forefinger to enter a cavity which was found to contain a foreign body. This, upon removal, proved to consist of a ball of hair the size of a small walnut, partially covered with a phosphatic deposit (Fig. 3). A tampon was inserted to the reflection of the peritoneum from the bladder and into the prevesical space. The wound was sutured with the exception of the cystostomy opening into which a Pezzer catheter was placed.

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The physicochemical and microscopic analyses of the stone showed it to be of homogeneous structure and composed of ammonium-magnesium phosphates.

Subsequent Course.—The patient made an uninterrupted recovery. The tampons were removed on the sixth day after operation. On the eighth day, the sutures were removed. The Pezzer catheter was taken out on the twelfth day and a Nélaton catheter *à demeure*

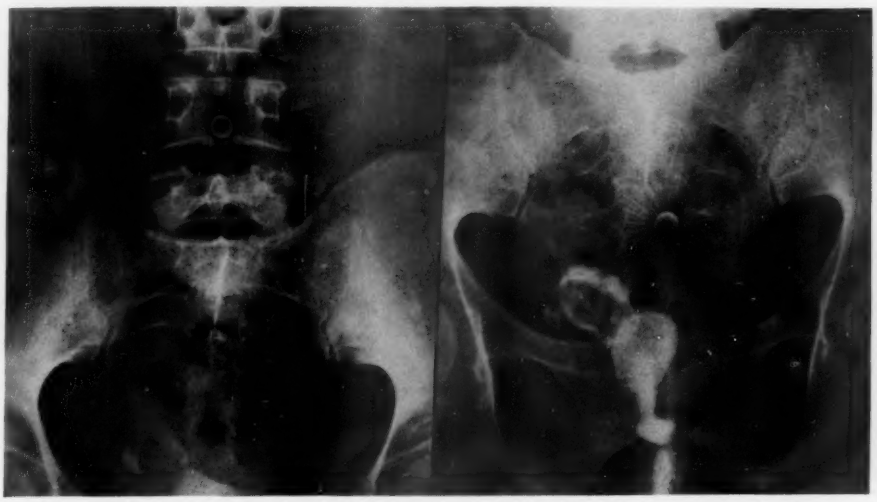

FIG. 1.—Primary roentgenogram showing a dense, mesially situated homogeneous shadow; and a second one of irregular density, partially superimposing the right upper aspect of the first shadow.

FIG. 2.—Preoperative cystogram: There was no alteration of the denser, mesial shadow, but the second, more poorly defined shadow, became considerably larger and its contour and anatomic relations much more definite.

introduced through the urethra. Urine ceased to come through the cystostomy wound on the fourteenth day and was discharged exclusively through the catheter. The catheter *à demeure* was removed on the seventeenth day. At the end of two weeks, the cystostomy wound had healed completely. The urine still contained red and white blood cells, but the symptoms of cystitis had ceased and the patient, who had been bereft of sleep and had frequently had to void small amounts of fetid, turbid urine, accompanied by intense pain, began to pass a clear odorless urine five to six times during the 24 hours.

FIG. 3.—Photograph of the gross specimens removed from the bladder and the cyst cavity, arranged in their relative positions.

Postoperative Cystoscopic Examination.—Bladder contents 300 cc.; mucous membrane reddened; vessels blurred; both ureter orifices normal. Intravenous indigo carmine returned in seven minutes in good concentration from each kidney. In addition, on both sides of the orifice of the right ureter and a little above it, two small excavations were seen, one the size of a small bean, the other the size of a pea, and between them a third small crater-like excavation with somewhat everted, folded edges. Probing with an ureteral catheter showed that the lateral excavations were very shallow, ¼ cm. deep, while the catheter could be introduced a distance of 3 cm. into the middle orifice. A

cystogram, employing 60 cc. of 10 per cent abrodil, revealed the shadow of the bladder to be the shape of an equilateral triangle with a truncated apex pointing upwards and a small spherical shadow, situated to the right of the base line, which apparently connected with the bladder cavity and was interpreted as representing the contracted cyst which had originally contained the hair ball (Fig. 4).

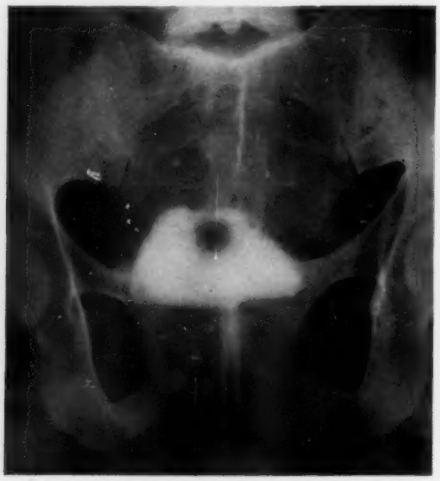

FIG. 4.—Postoperative cystogram: The residual, contracted cyst is represented by the small, spherical shadow, situated to the right of the base line of the vesical shadow.

SUMMARY

A female, age 30, suffering from an intractable cystitis, was impossible to cystoscope. Roentgenologic examination showed two shadows in the pelvis. Cystostomy revealed that one of the shadows corresponded to a stone, the other to a hair ball. The latter lay in a diverticulum which represented a paravesical dermoid cyst which had opened into the bladder. The cystovesical, fistulous tract having been dilated and its contents removed, the cyst became practically obliterated.

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CYSTS OF THE URACHUS

REPORT OF TWO CASES

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THE URACHUS is a structure which passes upward from the bladder toward the umbilicus. It is frequently referred to in anatomies as the middle umbilical ligament.[1, 2] Begg[3] has demonstrated that it is normally incompletely patent throughout life, and in several cases a continuation of the bladder mucosa into the urachus has been found. It is subject to the same pathologic processes which are noted elsewhere; namely, maldevelopmental, inflammatory, neoplastic and degenerative.

The most frequent abnormalities which are seen are: (1) Anomalies in development; (2) cyst formations, which may at times be related to congenital defects. Long[4] has classified cysts of the urachus into four anatomic groups:

(I) Those which communicate with the bladder.
(II) Those which communicate with the umbilicus.
(III) Those which communicate with the bladder and with the umbilicus, forming vesico-umbilical fistulae.
(IV) Those which do not seem to communicate with either (Plate I).

The present communication will confine itself, for the most part, to Group IV. These patients frequently present the diagnostic problem of differentiating a midline suprapubic mass which is only slightly movable. As infection is usually present, the mass is tender to palpation and the patient may appear acutely ill. The diagnosis is often made at the operating table, and the procedure to be performed is usually decided upon at this time.

Cysts belonging to the other groups will be considered if, due to closure of their drainage tract, they become potentially Group IV cases.

Incidence.—The incidence of cysts of the urachus is rather small. Young[5] reports only three cases in 12,500 admissions to the Brady Urological Institute. We have records of only four cases during the past five years. In 1886, Lawson Tait[6] presented 12 cases of suprapubic cysts, several of which were without doubt urachal in origin. They were all described as lying extraperitoneally. In two of these cases, excision was attempted, which resulted in immediate postoperative fatality. In the remainder, incision and drainage were effected, with no immediate mortality, although several deaths were later noted. Among the cases which lived, Tait did not describe any subsequent recurrences. He was probably the first surgeon to diagnose this condition preoperatively.

A complete analysis of the reported cases was published by Weiser,[8] in 1906. He states that, in 1648, Peu described a mass in a newborn child which

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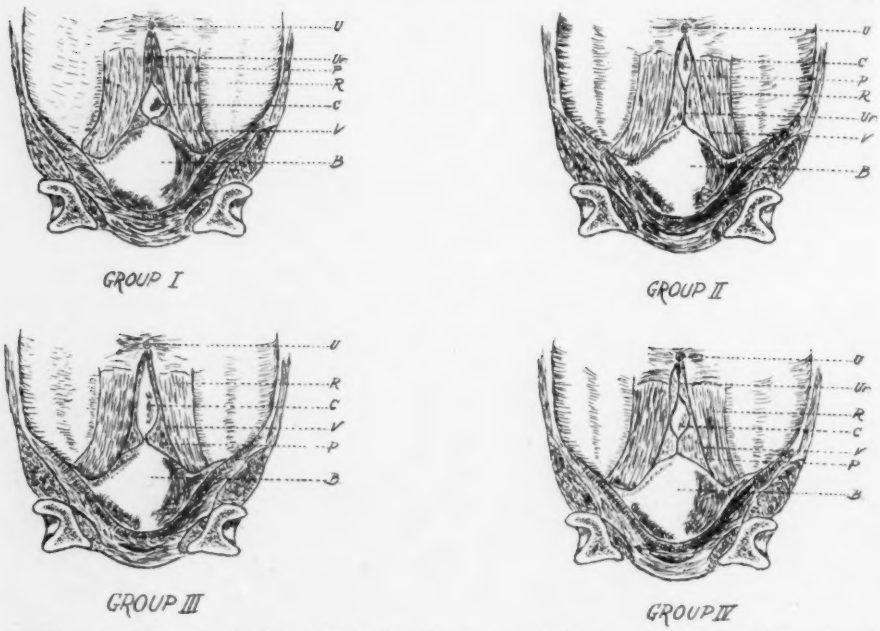

PLATE I.—Schematic drawings illustrating the four anatomic groups as suggested by Long.[4] U. Umbilicus. Ur. Urachus. R. Rectus muscle. P. Peritoneum. C. Cyst. V. Umbilical vessels. B. Bladder.

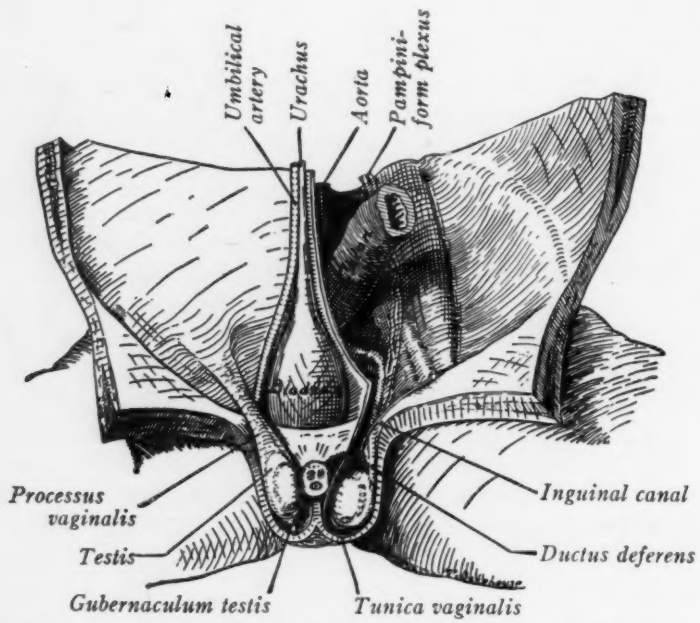

FIG. 1.—Ventral dissection of a nearly full-term fetus to demonstrate the relation of the descended testis to the processus vaginalis (after Corning). On the right the peritoneum is intact; on the left the peritoneum and its scrotal sacculation have been opened and the testis rotated 90°. (After Arey, L. B.: Developmental Anatomy, 2nd Ed. W. B. Saunders Co., Phila., p. 244, 1931.)

may have been due to a cyst of the urachus. The reports in the early literature were collected by Wutz,[7] in 1883. However, many of these early descriptions were considered inadequate for a positive diagnosis.

Embryology, Anatomy and Pathology.—The bladder is formed from the ventral portion of the cloaca, and is mesodermal in origin.[9] With growth and development, it later occupies a roughly triangular space with its apex at the umbilicus (Fig. 1).

The elongated apex, continuous at the umbilicus with the allantoic stalk, is the urachus.[10] As the bladder and the urachus descend, the attachment to the umbilicus is retained either as a fascial plexus or as a fibrous cord. Embryologically, the vesical epithelium is continuous into the urachus. This

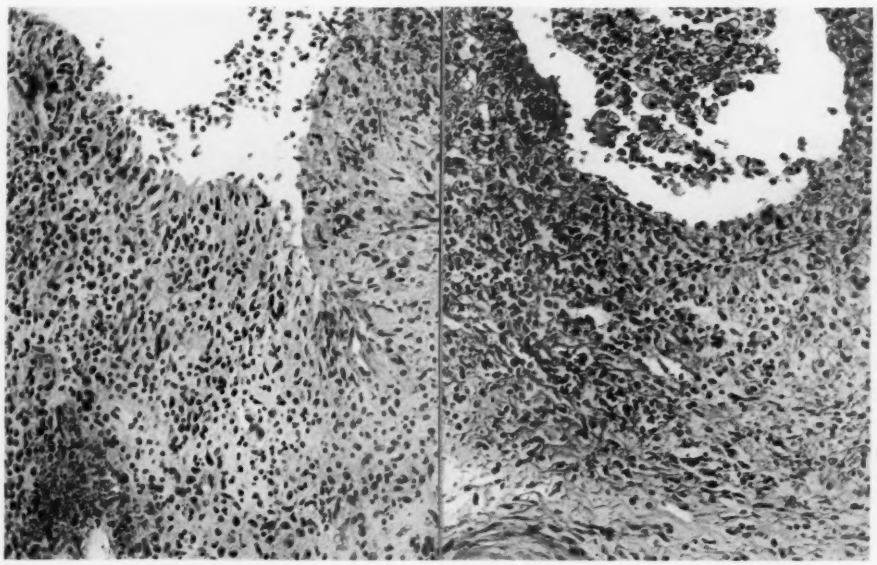

FIG. 2.—Case 1: Section of biopsy. Photomicrograph demonstrating replacement of epithelial lining by granulation tissues showing evidence of inflammation.

FIG. 3.—Section of specimen removed at autopsy. Photomicrograph showing evidence of inflammation and absence of epithelial lining of urachus.

was also confirmed in the comparative studies made by Rossi.[11] The lumen of the urachus is never entirely obliterated, and occasionally secretory cells have been demonstrated in the mucosa. Begg[12] has also pointed out that there is a more or less constant tendency for epithelial desquamation.

In considering the pathogenesis of cysts, two possibilities may be pointed out. There may at times be protrusion of mucus-secreting cells into the wall of the urachus. These are shown in Begg's[12, 13] sections. Probably the more common method is the closure of the lumen by débris, with accumulation of secretions and consequent cyst formation.

At operation, most of the cysts are obviously infected. In those forming Group IV, it is interesting to speculate as to the avenue of infection. Hematogenous and lymphogenous spread have been suggested, and these possibilities

are not to be denied. However, with previous communication with the bladder demonstrated, direct extension seems plausible in most cases. The tract may not be demonstrated because of subsequent obliteration. Powell[14] reported a case where, with closure of the urachal communication with the bladder, an infected cyst was formed. This case was cured by incision and drainage.

Cultures from infected cysts are not infrequently reported sterile. However, this is in accord with localized infections elsewhere which, after a period of time, may become sterile. *Bacillus coli communis,* Streptococcus and Staphylococcus have been reported present.

Microscopic study of a section of cyst wall from Case I showed the replacement of the mucosa by inflamed granulation tissue (Fig. 2). In the study of an infected cyst of the urachus noted as an associated finding during a recent autopsy, it was again found that the mucosa was replaced by granulation and fibrous tissue (Fig. 3). This probably accounts for the frequent absence of recurrence following incision and drainage of infected cysts.

Surgical Procedure.—In reviewing the literature on cysts of the urachus, one finds that the diagnosis is usually made at operation. Following the usual suprapubic incision the mass is observed to be extraperitoneal, and its origin from the urachus is frequently obvious. Because of the conception held by several surgeons that complete extirpation is necessary for cure, the following case is presented.

CASE REPORTS

Case 1.—M. R., female, age 2, was admitted July 23, 1937, to the service of Dr. E. Beer, Mount Sinai Hospital. Her mother stated that for the past week the child had appeared ill. She had vomited several times, but no fever was noted. For two days prior to admission, the child cried during and after urination. Temperature 101.2° F. For 24 hours, the child had voided small quantities, and catheterization yielded about five ounces of "strong-smelling" urine. After completely emptying, the physician noted that the "bladder remained tense." Past history was irrelevant. There had been no illnesses related to the urinary tract.

Physical Examination revealed an acutely ill, fretful child. Except for the abdominal findings, no abnormalities were noted. In the suprapubic region, and extending midway to the umbilicus, was a round, somewhat tender, cystic mass about the size of an orange. It was not freely movable, but could be displaced slightly from side to side. During the examination, the child expressed a desire to void, and passed about 20 cc. of clear urine. There was no apparent pain during micturition. The mass descended slightly toward the symphysis but did not decrease in size. Uranalysis and blood chemistry normal. Wassermann reaction negative. A plain roentgenogram of the abdomen and a pyelogram, following injection of hippuran intravenously, were reported normal.

Cystoscopic Examination.—Dr. M. Swick: As the bladder was filled, it was noted that the mass, retaining its original size, rose upward toward the umbilicus. The bladder mucosa was entirely normal, and no diverticula were seen. As the bladder was emptied, there seemed to be intrusion of an extravesical mass on the superior wall of the bladder. This was coincident with the descent of the mass as noted abdominally. Dr. A. Hyman suggested an infected urachus cyst among the possible diagnoses.

Operation.—A midline suprapubic incision was made into a cyst which contained about eight ounces of thick, creamy pus. Evacuation of the contents revealed a smooth-walled cavity from which a biopsy was taken. The cyst was drained. *Pathologic Diag-*

nosis: Dr. Paul Klemperer. Biopsy specimen: Inflamed, fibrous cyst wall (Fig. 2). Culture: Negative.

Convalescence was uneventful. The patient was discharged August 4, 1937, the seventeenth postoperative day, with the wound practically healed.

When seen in the Follow-Up Clinic, six months later, the scar was firm and there was no evidence of recurrence or herniation. The cure effected by this simple procedure was unquestioned.

The following case of Dr. A. A. Berg is reported:

Case Report.—S. M., male, age 29, physician, was admitted to the Mt. Sinai Hospital March 20, 1935, complaining of a tender, suprapubic swelling, which had been present for some time. There was a persistent low grade fever, and he had suffered some loss of weight. *Preoperative Diagnosis:* Suppuration of the urachus.

Operation.—Dr. A. A. Berg: The mass was incised by a suprapubic midline incision, and several loculated abscess cavities were found. These contained foul-smelling pus, and drainage was instituted.

Convalescence was complicated only by persistent drainage from a remaining sinus. The patient was discharged, April 20, 1935, in good physical condition. However, the sinus continued to drain, and the patient was readmitted June 23, 1935, for excision of the tract. At this operation it was noted that, except for one small pocket of pus, the wound was clean and healed. Fibrous and granulation tissue had completely obliterated the cavity. It was suspected that the sinus led down to the bladder, and excision of the cyst was performed. A connection with the bladder could not be demonstrated during the procedure. The postoperative course was again complicated by continued drainage from the wound. At the end of several months, the wound showed no evidence of closing, and the drainage still continued to be profuse. The sinus tract was now injected with radiopaque oil, and roentgenologic examination demonstrated a communication with the bladder and a branching sinus running into the abdomen toward the ileocecal region. The urine was grossly infected, and the sinus discharge was foul.

The patient was readmitted to the hospital for an exploratory celiotomy. At operation, the intra-abdominal sinus was traced to an old gangrenous appendicitis with abscess cavity. This was removed with great technical difficulty. To control the severe cystitis, suprapubic cystotomy was performed. The patient improved rapidly, and was discharged October 2, 1936. The sinus leading to the base of the appendix was closing, and the patient's condition was good.

Follow-Up: Convalescence was uneventful except for the persistence of a small fecal fistula, which is still present. Its etiology has remained somewhat obscure, and the patient is to be restudied. His health has remained excellent and there have been no residual urinary symptoms.

The patient, in retrospect, dated the onset of the appendicitis to an attack of severe right lower quadrant pain which he had suffered some time prior to the third operation. However, Dr. Berg's description of the healing wound, present at the time of the second operation, clearly indicated the advantage of this initial procedure.

A review of the reported cases of cyst of the urachus proved most interesting in determining the necessity of complete excision of the cyst for permanent cure. Because of changes in operating room technic, only cases reported since the publication by Weiser[8] are presented in the table. Group IV cases were chosen because the diagnosis was usually obscure and the operative technic of excision is frequently difficult.

TABLE I

CYSTS OF THE URACHUS REPORTED IN THE LITERATURE FROM 1907–1936

No.	Reported by	Year	Age	Sex	Group	Diagnosis	Infection	Operative Procedure	Result	Drainage Period	2nd Operation
1.	Macdonald[16]	1907	40	F.	IV	Operation	?	Excision*	Cured	—	—
2.	Doran[17]	1908	17	F.	IV?	Operation	No	Excision of anterior wall. Drained	Cured	Not stated	—
3.	Arrou[18]	1910	?	M.	II?	Preoper.	Yes	Excision	Cured	—	—
4.	Cullen[19]	1910	15	M.	IV	Operation	Probable	Incised and drained	Cured	Not stated	—
5.	Weber[20]	1910	26	F.	IV?	Operation	?	Excision	Cured	—	—
6.	Baldwin[21]	1911	6	F.	IV?	Operation	No?	Incised and drained	Cured	Brief	For incisional hernia
7.	Baldwin[21]	1901	33	F.	IV	Operation	Yes	Incised and drained	Cured	Prolonged. Cyst large	—
8.	Means[22]	1914	32	M.	IV	Preoper.	No	Excision	Cured	—	—
9.	Boni[23]	1914	23	M.	IV	Preoper.	No	Excision	Cured	—	—
10.	Jacoby[24]	1915	33	F.	IV	Operation	?	Anesthetic death	—	—	—
11.	Morone[25]	1915	17	F.	IV	Preoper.	Yes	Incised and drained	Cured	3 mos.?	—
12.	Gramen[26]	1916	41	M.	IV	Operation	Yes	Excision	Cured	—	—
13.	Aleman[27]	1916	51	M.	IV	Operation	Yes	Excision?	Died. Peritonitis	—	—
14.	Ward[28]	1918	44	F.	III?	Preoper.	Yes	Incised and drained. Concretion removed	Cured	10 days	—
15.	Davis[29]	1919	33	M.	I? IV?	Preoper.	Yes	Excision	Cured	14 days	—
16.	Bua[30]	1920	35	F.	IV?	Operation	?	Excision*	Cured	—	—
17.	Edington[31]	1921	50	M.	IV	Operation	No	Excision*	Cured	—	—
18.	DeCastro[32]	1926	24	F.	IV?	Operation	Yes	Excision*	Cured	—	—
19.	Rankin and Parker[33]	1926	55	F.	IV?	Operation	Yes	Excision	Died. Peritonitis	—	—
20.	Rankin and Parker[33]	1926	20 mos.	F.	I? IV?	Probable	Yes	Drainage tract dilated	Not followed	—	—
21.	Lubash[34]	1929	22	M.	II?	Preoper.	Yes	Emergency excision	Cured	Prolonged	—
22.	Denneen and Margold[35]	1929	43	M.	IV	Operation	Yes	Celiotomy for peritonitis	Died	—	—
23.	Ronald[36]	1929	26	M.	IV?	Operation	No	Excision	Cured	—	—
24.	Tassovatz[37]	1930	23	M.	II? IV?	Operation	Yes	Excision	Cured	Brief	—
25.	Siddall[38]	1931	24	F.	IV	Operation	No	Incomplete excision	Cured	Brief	—
26.	Long[4]	1931	5	M.	IV?	Preoper.	Yes	Incised and drained	Cured	3 wks.	—
27.	Long[4]	1931	6	M.	II?	Preoper.	No	Excision	Cured	Brief	—
28.	Long[4]	1925	27	F.	IV?	Operation	Yes	Spontaneous rupture. Drained	Cured?	Brief	—
29.	Bauer[39]	1931	47	F.	IV?	Operation	?	Excision	Cured	—	—
30.	Schmidt[40]	1933	24	M.	IV?	Operation	No	Excision	Cured	—	—
31.	Rives[41]	1933	?	M.	IV?	Preoper.	Yes	Incised and drained	Improved	2 mos.	Excision
32.	Stevens[42]	1933	24	M.	IV?	Preoper.	Yes	Excision	Cured	—	—
33.	Lazarus and Rosenthal[43]	1933	51	M.	IV	Operation	Yes	Excision	Died. Peritonitis?	—	—
34.	Ginsburg and Nixon[44]	1934	2	F.	IV	Preoper.	Yes	Excision	Died. Peritonitis	—	—
35.	Gayet and Verriere[45]	1935	69	M.	IV?	Operation	Probable	Excision*	Not stated	—	—
36.	Lavand'homme[46]	1936	22	F.	IV?	Operation	Yes	Incised. Cyst marsupialized	Improved	1 mo.	Incomplete excision. Curettement

* Operation reported to be technically difficult. Peritoneum excised with adherent cyst wall. Bladder opened in some cases. Closure of the abdomen was occasionally nadequate.

EXPLANATORY NOTES RELATIVE TO CASES CITED IN TABLE I

Case 1.—Excision undertaken only because of suspicion of carcinoma; not corroborated by microscopic study. Procedure difficult and postoperative course stormy.

Case 2.—Excision not practical. Posterior cyst wall left.

Case 6.—Patient reoperated upon four months later for incisional hernia. The note of the surgeon's findings are recorded elsewhere.

Case 10.—On attempted excision at postmortem, the surgeon stated it would have been too difficult to perform.

Case 21.—At previous celiotomy, the cyst was said to have ruptured intraperitoneally, and drainage was instituted. Injection of the sinus for roentgenologic purposes resulted in peritoneal reaction and immediate excision was performed. Convalescence was stormy.

Case 22.—At celiotomy, peritonitis was found. Autopsy revealed its etiology to be an unusual intra-abdominal perforation of an infected urachus cyst.

Case 31.—Continued drainage of serous fluid was not explained. Secondary excision was reported as having been relatively easy.

Case 33.—Celiotomy was performed first, with negative findings. Mass was excised and pus was noted to extend into the groin. Anuria developed, with death from uremia.

Occasionally where portions of cyst wall were left, various methods for cauterization were employed.

ANALYSIS OF CASES CITED IN TABLE I

Seven cases of cure following incision and drainage of the cyst were recorded. In all but one, infection was definitely present. Three cases of incomplete excision with cures were noted. No recurrences in these cases have been reported.

Four cases with fatality subsequent to excision are recorded. In three of these, peritonitis was given as the cause of death.

Four cases of excision secondary to initial incision and drainage were presented. In three of these, complicating features as noted may have prevented normal healing.

In many of the reports, where primary excision was performed, technical operative difficulty was noted. Adherent peritoneum was frequently excised, with occasional difficulty in closure. The bladder was opened in several instances. In one report, attempted excision would have been futile.

Case 6 (Baldwin[21]), reoperated upon for incisional hernia, four months after incision and drainage, the surgeon stated: "The sac had entirely disappeared and nothing was found to suggest previous trouble in the abdomen."

SUMMARY.—(1) Cysts of the urachus are conveniently classified by an anatomic grouping.

(2) A review of the Group IV cases, from the recent literature, is presented.

(3) Two additional cases are reported.

(4) Microscopic sections demonstrating destruction of the epithelial lining of the urachus in the presence of infection are shown.

CONCLUSIONS

It is suggested that where the diagnosis of infected urachus cyst is made, incision and drainage may be adequate to effect a cure.

Where reoperation may be necessary, subsequent excision is more easily and safely performed.

Appreciation is expressed to Drs. A. A. Berg, R. Lewisohn, P. Klemperer and A. Pollock for their kind assistance.

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WHOLE-THICKNESS GRAFTS IN CORRECTION OF CONTRACTURES DUE TO BURN SCARS*

THREE CASE REPORTS

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THE surgical correction of a deformity of the trunk or extremity resulting from the contractural effect of a deep burn scar presents a most difficult problem. Because of the continued contracture of such a cicatrized area, the scars overlying joints tend to cause increased deformity in time and, in young subjects, the growth of the individual may contribute toward the development of crippling disability. The continued trauma coincident to locomotion or other exercise causes these unstable scars to ulcerate readily. The epithelium overlying the scar is thin; the blood vessels are few; and stretching of the scar in an attempt to correct the deformity, as is often practised in the methods of physical therapy, produces ischemia which may be followed by ulceration.

In cases in which the scarred area is not too large, the thickened scars may be excised completely and the superficial defect repaired with large grafts of skin. Blair and Brown[1] have advanced this form of treatment, and have reported many cases in which large scars have been completely replaced by thick-split grafts of skin. When, however, complete excision of the scarred tissue is not feasible by reason of the magnitude of the deformity or the paucity of cutaneous areas from which grafts may be cut, some other method must be adopted. In such cases it has been my practice to combat the contractural effect of the scar by the interposition of an elliptically shaped, whole-thickness, free graft of skin at a strategic point in the line of pull of the scar. A simple, linear, relaxation incision is made in such a way as to divide the scar at the point where it exerts greatest force. Such an incision establishes an elliptical, gaping wound into the floor of which the normal fatty or muscular tissue bulges. Scar tissue remnants are dissected away from the edges of the wound. A whole-thickness, free graft of skin, patterned to fit the defect, is introduced. The graft is sutured accurately into place and held immobilized by a dressing incorporating sponge rubber. Because the successful transplantation of large, whole-thickness grafts of skin depends largely on complete immobilization of the wound in the early postoperative period, a suitable plaster spica is applied. The reward of adequate postoperative immobilization of the area is a complete "take" of the graft. When healed, the transplantation forms an elastic bridge at the midpoint of a contracture upon which both sections of the scar may exert their force. Because of its elasticity, its mobility, and

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its resistance to potential contractions, the whole-thickness graft of skin is preferred, although the details of operation and after-care are more burdensome than those of the Ollier-Thiersch or thick-split graft. Split grafts of skin, if applied to a soft tissue surface, undergo contraction evidenced by the development of wrinkles on the surface of the graft and by the subsequent decrease in width of the original relaxation incision.

ABBREVIATED CASE REPORTS

Case 1.—N. Y. Hosp. No. 73967: Massive burn scar of lower abdomen, groin and upper thigh; causing flexion contracture of thigh. H. H., male, age 10, while playing with fireworks, had been severely burned, five years previously, when his clothes caught fire. Examination, August 28, 1934, showed an extensive scar, measuring 32 cm. vertically and 20 cm. transversely, which extended from the midabdomen down to the midportion of the left thigh. Flexion deformity of the thigh measured 30 degrees. The scar was hard, pale and greatly thickened (Fig. 1).

Operation.—August 27, 1937: Under ether anesthesia a "relaxation" incision, 12 cm. long, was made parallel to Poupart's ligament. All the scar tissue was dissected away from the floor of the resultant elliptical wound, exposing the loose, areolar tissue overlying the femoral artery, vein and nerve. A whole-thickness graft was cut from just above the crest of the right ileum, according to a pattern of the wound, the resultant cutaneous defect being obliterated by undercutting the flaps and approximation of the edges. The graft was accurately sutured into place in the left inguinal region. A dressing, incorporating sponge rubber, was applied and immobilization was accomplished by means of a plaster hip spica. The graft was successfully transplanted, and "took" in its entirety. The patient was discharged on the seventeenth day postoperative.

Subsequent Course.—The flexion contracture of the thigh had been relieved (Fig. 2); the scar tissue above and below the graft had become softer and apparently thinner. Through the graft, the structures in the femoral triangle could be easily palpated.

Case 2.—N. Y. Hosp. No. 28343: Massive burn scar of right trunk and right thigh; causing partial scoliosis and flexion contracture of the thigh. M. C., female, age 12, had been severely burned six years previously, when her clothing caught fire. Examination, February 2, 1937, showed extensive, deep scars running from the scapular and axillary regions down the thoraco-epigastric region to the lateral and anterior aspects of the right thigh. A linear band of scar tissue was noted in the thoracolumbar region. Just inferior to the crest of the ilium, the scar was very thick and at this point it was adherent to the underlying bone (Fig. 3).

Operation.—December 21, 1937: Under ether anesthesia, "relaxation" incision, 10 cm. long, was made over the crest of the ilium. All scar tissue was dissected away from the floor of the resultant elliptical wound. A whole-thickness graft of skin, measuring 4x11 cm., was cut from the region of the left gluteal fold, according to a pattern of the wound. The graft was sutured in place and the donor site was closed by primary suture. Guttapercha was placed over the graft and moderate pressure was made on it by tight adhesive strapping over a layer of rubber sponge. Immobilization of the extremity and lower torso was accomplished by means of a plaster hip spica. The graft was successfully transplanted (Fig. 4), except for an area, 2x2 cm. in size, in its anterior portion where complete sloughing occurred. This was apparently due to the marked ischemia of the adjacent scar. A Z-plastic operation was performed in the lateral thoracic region (Fig. 5). The patient was discharged on the twenty-fifth day postoperative.

Subsequent Course.—The scoliosis has been corrected (Fig. 5). The flexion contracture of the thigh will be cared for subsequently.

Case 3.—N. Y. Hosp. No. 182097: Annular burn scar of thigh of 22 years' duration; with ulceration and impairment of venous circulation of the leg. F. G., male, age 34, re-

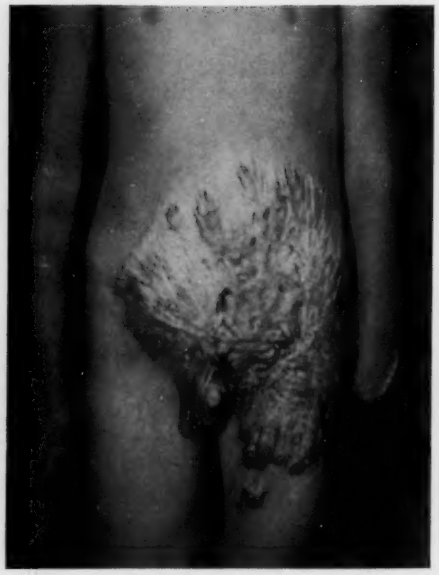

FIG. 1.—Case 1: Massive burn scar of lower abdomen and thigh. The scar was hard, pale, and approximately 2.5 cm. deep. Extension of the thigh was limited 30 degrees. On forced extension of the thigh, the scar became white in the area overlying Poupart's ligament.

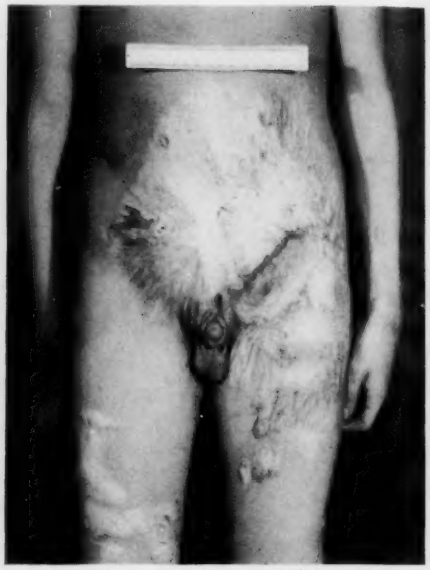

FIG. 2.—Case 1: Whole-thickness graft in place where "relaxation" incision was made over Poupart's ligament. After operation, the scar became softer and thinner and extension of the thigh was no longer limited.

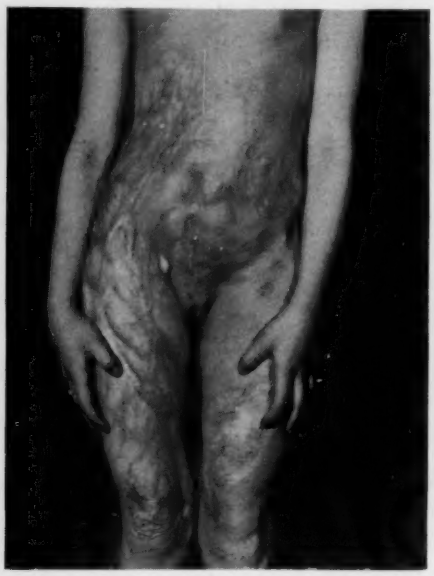

FIG. 3.—Case 2: Dense burn scar of right thoracic and abdominal wall and right thigh. Scoliosis and limitation of extension of the thigh were the major deformities.

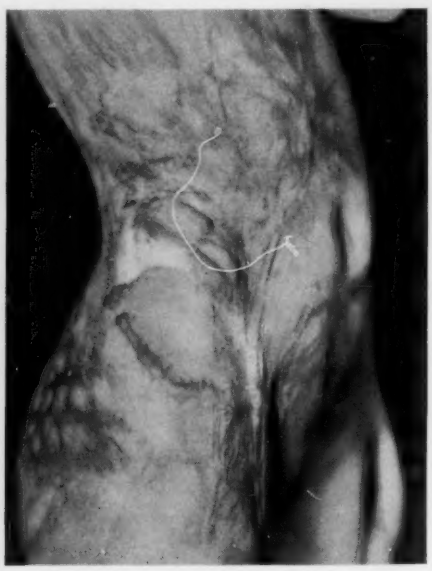

FIG. 4.—Case 2: Photograph taken after operation, to show the extent of the whole-thickness graft of skin. The pull of the scar tissue band, in the anterior portion of the thigh, will be corrected at a future operation.

ceived severe dynamite burns of the right thigh at age 12. He was hospitalized for 13 months, during which time skin grafts were applied to the wound on several occasions, without success. Six years elapsed before the wound was entirely covered with scar epithelium. Four years ago, the patient was accidentally cut on the outer aspect of the right thigh. The ulcer which resulted persisted until the time of his admission to the New York Hospital. The patient had moderately severe diabetes.

Examination, March 3, 1938, showed an extensive deep scar of the anterior and lateral aspects of the upper right thigh. Its contractural effect was evidenced by an annular depression of the inner and posterior aspects of the thigh and the numerous large varicosities below the level of the scar. On the lateral aspect of the scar, there was a punched-out ulcer, 2x3 cm. in size (Fig. 6). Over the anterior thigh, a small sinus discharged frag-

FIG. 5. FIG. 6. FIG. 7.

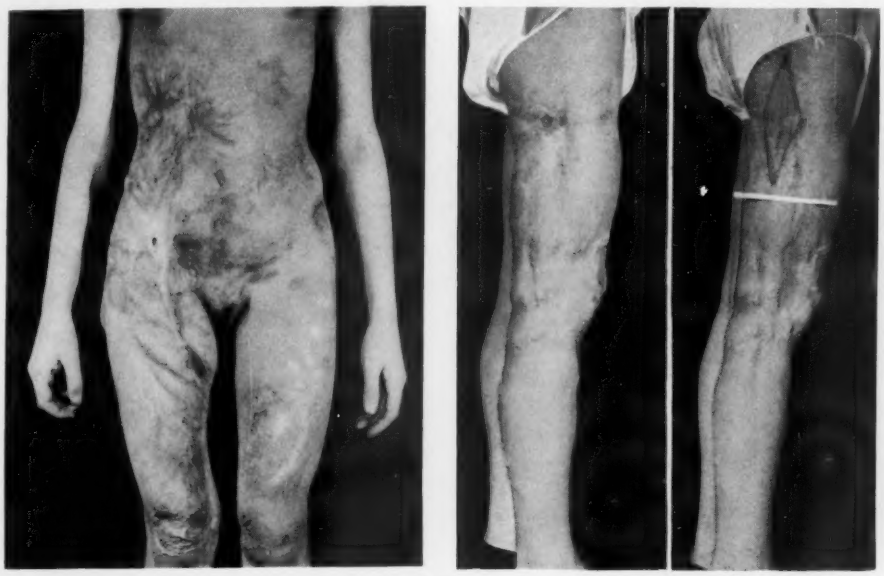

FIG. 5.—Case 2: Photograph taken after Z-plastic operation upon lateral abdominal area; "relaxation" incision just below the crest of the ilium; and insertion of an elliptical, whole-thickness graft of skin. Note the correction of the curvature of the spine.

FIG. 6.—Case 3: Annular burn scar of the leg, with ulceration and obstruction to the superficial veins causing varicosities. Scar had been present for 22 years.

FIG. 7.—Case 3: Photograph taken 30 days after operation, at which time the ulcer was excised; "relaxation" incision was made, and whole-thickness graft of skin was introduced. The diminution in the extent of the varicose veins is very striking.

ments of calcified fibrous tissue. Extension of the thigh in walking caused pallor of the scar.

Operation.—March 18, 1938: Cyclopropane anesthesia. After adequate dakinization of the ulceration and regulation of the diabetic state, the ulceration on the lateral aspect of the thigh was removed by an elliptical incision. The scar tissue was 1.2 cm. thick. A "relaxation" incision, 18 cm. long, was made parallel to the long axis of the thigh. The floor of the wound was freed of fibrous tissue, so that healthy, adipose tissue bulged into the defect. An elliptical free graft of the whole-thickness of skin was cut from the right lateral abdominal region according to a pattern of the wound. The donor wound was closed by linear approximation of the edges of the skin after adequate undercutting. The graft, measuring 8x20 cm., was sutured into place in the wound on the thigh and held immobilized by a dressing incorporating sponge rubber. A plaster hip spica was applied. The patient was discharged on the thirtieth day postoperative.

Subsequent Course.—On opening the dressing, 12 days after operation, it was apparent

that the graft had taken. Two small areas showed superficial sloughing. The patient was allowed to walk about after four weeks of bed rest. There was a complete release of tension in the thigh, the varicosities were less in evidence (Fig. 7), and the patient enjoyed much greater freedom of motion in the extremity.

Discussion.—The interruption of a contracture due to a burn scar by "relaxation" incision, and the insertion of a whole-thickness free graft of skin, has been found to be an effective method of correcting skeletal deformity due to burn scars. This method of surgical treatment was referred to by Davis,[2] as early as 1917. Since then, the surgical literature has shown so many reports of the treatment of dense burn scars by the use of pedunculated flaps of skin and subcutaneous tissue, that the impression prevails that such deformities cannot be corrected without long periods of hospitalization and operation in several stages. The method employed in these three cases is most ideally applicable to scars about the trunk and extremities in which a maximal, functional end-result is the aim, and the cosmetic result is relatively unimportant.

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[2] Davis, John Staige: Surg. Gynec., and Obst., **25**, 1, 1917.

PILONIDAL SINUS

SACROCOCCYGEAL ECTODERMAL CYSTS AND SINUSES

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CYSTS occurring in the sacrococcygeal region having cutaneous openings on the skin surface are of frequent occurrence. These sinuses and cysts have been grouped under the inappropriate and nondescriptive term, "pilonidal sinus." The term "pilonidal" is derived from the Latin and simply means a hair nest. Hair nest has no significance and is certainly not descriptive of this interesting clinical entity. Most authors agree regarding the etiology—namely, that these cysts and sinuses result from a maldevelopment of the ectoderm—but they disagree as to the primitive structure from which they originate. As a more descriptive term is desirable, the author proposes the name "sacrococcygeal ectodermal cysts and sinuses." The term denotes not only the character of the lesion but its derivation as well. This descriptive phrase can with equal lucidity be applied to both the sacrococcygeal sinuses and sacrococcygeal dimples.

Consideration of the etiology of these pathologic clinical entities has been both interesting and disappointing; interesting from the ingenuity of the theories, and disappointing from the practical application by the profession. To review all of the theories would be time-consuming and without profit; therefore, the reader is referred to articles by Gage,[1] Fox,[2] and Stone,[3] for detailed description of the etiologic factors.

From an embryologic and clinical review the author has divided the pilonidal sinuses and cysts into four groups, as follows: Group I.—(A) The simplest of all the types—the sacrococcygeal dimple; and (B) its counterpart, sacrococcygeal dimple sinus. Group II.—All true pilonidal cysts and sinuses and their ramifications that are confined to the sacrococcygeal region without entering the sacral canal. Group III.—All true pilonidal cysts and sinuses, multiple or single, that enter the sacral canal but are not continuous with the central canal of the cord or the subarachnoid space, but may be attached to the dura. Group IV.—The rarest of all the true pilonidal cysts and sinuses, those that enter the sacral canal or pass through a defect in the sacral vertebrae and become continuous with the central canal of the spinal cord or open into the subarachnoid space. In Group IV, cerebrospinal fluid is discharged from the external opening of the sinus (Moise,[4] and Ripley and Thompson[5]).

Pathology.—The gross pathologic manifestations of pilonidal sinus are more or less constant. There are single or multiple sinus openings which connect with cystic dilatations located subcutaneously. The cystic dilatations

are of various types. The sinuses may extend deeply toward the sacrum and a bulbous dilatation be present at its distal end. In this type the cystic dilatation is in close association with the periosteum over the sacral hiatus or extends upward over the sacrum. There may be two cystic dilatations, one just beneath the dermal layer of the skin which is connected with the other cystic dilatation which is in juxtaposition with the periosteum over the sacral hiatus or the lower sacrum. When the cystic dilatation is comparatively large there are multiple sinus connections with the skin surface. Occasionally one will find a small subdermal cyst that has no sinus opening on the skin surface. In cases of the latter type there will be a very small bluish area, 1 to 2 Mm. in diameter. This bluish area is due to covering over the sinus with a scant layer of epithelium. Surrounding the cysts and sinuses there is a slight tumefaction due to surrounding inflammatory reactions. If serial sections 5 cm. thick are made of the removed specimen the small sinus with slight dilatation or a wide cystic dilatation can be seen (Fig. 1). In rare instances the sinus tract enters the sacral canal through the sacral hiatus or through a defect in the bony covering of the canal. This sinus may then either be attached to the dura or continuous with the canal of the cord or subdural space. That part of the sinus tract entering the canal may have cystic dilatations of the lumen.

FIG. 1.—Photograph of gross serial sections of completely removed pilonidal sinus, demonstrating the cystic dilatations in the lower segments. The sinus tract is surrounded by a zone of granulation tissue.

The most frequent complication of pilonidal sinus is an acute infection with abscess formation, which may be either single or multiple. The infecting organism is predominantly the Staphylococcus; however, the colon bacillus is not an infrequent contaminator. When the abscess is incised or ruptures spontaneously it leaves a discharging sinus. These abscesses with their secondary sinus formation are located in the majority of instances to either side of the midline. When an abscess or secondary sinus is located on either side of the midline,

it indicates that the cystic dilatation of the pilonidal sinus is located deep below the overlying skin. In this position the cystic portion is very near the periosteum of the sacrum or the sacrococcygeal junction (Fig. 2). However, if the cystic portion of the sinus is located just beneath the skin surface the secondary sinus formation in the majority of instances occurs in the midline. When the cystic dilatation is just beneath the integument and an abscess develops in the cystic portion a sinus with granuloma formation invariably results (Fig. 3). Therefore, the relative position of the secondary sinuses will aid in determining clinically the location of the cystic portion of the sinus. Carbuncles, though they rarely occur as a complication, may have their origin in the overlying integument or develop from secondary

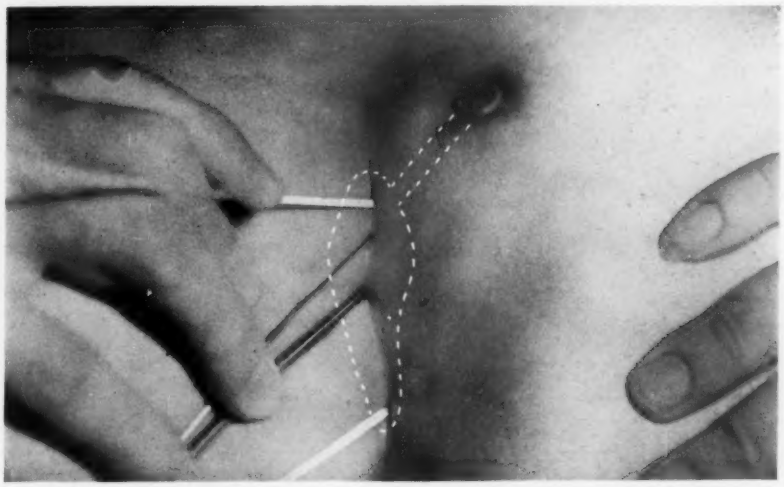

FIG. 2.—Photograph showing a deep seated cystic dilatation of a pilonidal sinus with secondary sinus formation. There are four primary openings and one secondary sinus opening, the latter containing a granuloma.

infection of the pilonidal sinus tract. We have had only one case in which a carbuncle complicated the pilonidal sinus.

The sacral dimple seldom results in the formation of a sinus. When sinus formation occurs it then falls heir to all of the inflammatory complications that occur in true pilonidal cysts. When an abscess complicates the sacrococcygeal dimple sinus with secondary sinus formation resulting, the latter is frequently mistaken for a fistula-in-ano.

Direction of the true pilonidal sinus and its cystic counterpart is cephalad. When multiple primary sinuses are present or secondary sinuses occur, their direction in the majority of instances is straight downward to the cystic counterpart. The direction of the sacrococcygeal dimple sinus, in contradistinction to the above, is caudal.

The miscroscopic study of the sinus and cyst is most interesting as regards their ectodermal lining, which is practically devoid of ectodermal appendages. The epithelial lining of both the sinuses and cysts is of the stratified squamous type (Fig. 4). The epithelial lining is seldom complete,

characterized by cracks, fissures, and shedded epithelium. These areas are filled in by granulation tissue. In some of the sinuses studied, desquamation of the entire epithelial lining occurred. When this condition exists, the lining is composed of granulation tissue surrounded by a wall of dense connective tissue. If abscess formation occurs in the sinus tract or its cystic portion, the resulting cavity is filled with granulation tissue, sinus formation occurs, and a granuloma results. Hair shafts and follicles are very numerous, having their origin from the ectodermal epithelial lining. The hair shafts

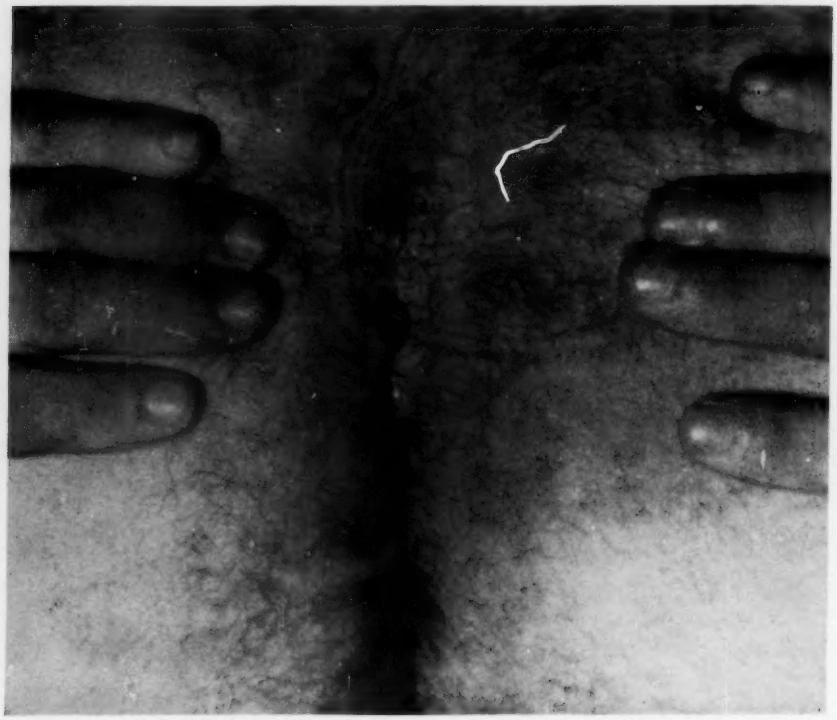

FIG. 3.—Photograph showing a pilonidal sinus secondarily infected, with a granuloma presenting in one of the openings of the sinus. In this case the abscess was located in the superficial cystic dilatation of the sinus.

are immature, frequently protrude from the sinus opening, and occasionally fill the cystic dilatation of the sinus. Hair shafts and hair follicles are the only ectodermal appendages which the author has been able to demonstrate. Although others have described sebaceous and sweat glands, the author has been unable to verify these findings. Sweat glands and sebaceous glands are occasionally seen in association with the pilonidal cysts and sinuses; however, they originate from the normal overlying skin. They penetrate downward and are in juxtaposition to the cyst and sinus. This arrangement is probably responsible for the misinterpretation of the authors who have described sebaceous and sweat glands as arising from the epidermoid lining of the pilonidal sinus.

In the sacral canal the epithelial lining is somewhat different from that which is superficial. Although the epithelial lining is of the epidermoid type, there is complete absence of hair follicles and hair shafts. The lining is a modified, stratified, squamous epithelium and is more typical of mucous membrane than skin.

All of these sinuses, both primary and secondary, reveal different degrees of inflammation, ranging from acute to chronic with concomitant fibrosis, which predominates in the chronic form. The inflammatory re-

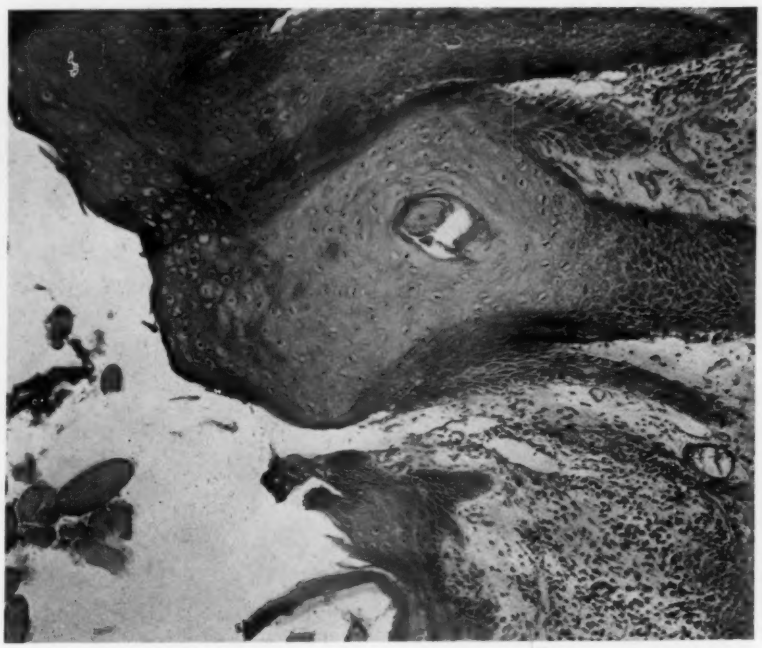

FIG. 4.—Photomicrograph illustrating the stratified squamous epithelial lining of the sinus tract as well as demonstrating the presence of hair shafts and follicles. Desquamation and fissuring of the epithelial lining is clearly seen in the center. There are no sebaceous or sweat glands present.

actions are characterized by subepithelial infiltration of the various inflammatory cells (Fig. 5). In the presence of abscess formation the cellular constituents are predominant of the polymorphonuclear variety, the acute reactions fading progressively as the distance from the sinus increases. Some distance from the acute reaction granulation tissue is present in varying amounts. In old cases of pilonidal sinus chronic inflammatory reaction predominates. This is characterized by extensive productive fibrosis with active granulation tissue near the lumen of the sinus. In fact, when abscesses have occurred with secondary sinus formation, the sinuses are filled with granulation tissue and the surrounding tissue is a wall of dense connective tissue. It is also common to find complete loss of epithelial lining. In this instance the lining of the sinus is granulation tissue mounted on a fibrous wall. This pathologic sequence is responsible for the granulomata seen in

association with pilonidal sinus, both primary and secondary. In the uncomplicated case, varying degrees of chronic inflammatory reactions are seen. Even in this type there are cracks and fissures of the epithelial lining, with complete deepithelialization in small areas of the tract. The inflammatory reaction in the uncomplicated case is confined in the majority of instances to the subepithelial area and is never extensive in its scope.

Clinical Manifestations.—In the average uncomplicated case of pilonidal cyst and the sacrococcygeal dimple sinus there are four signs and no symptoms, except slight pain or discomfort occasionally experienced by the patient.

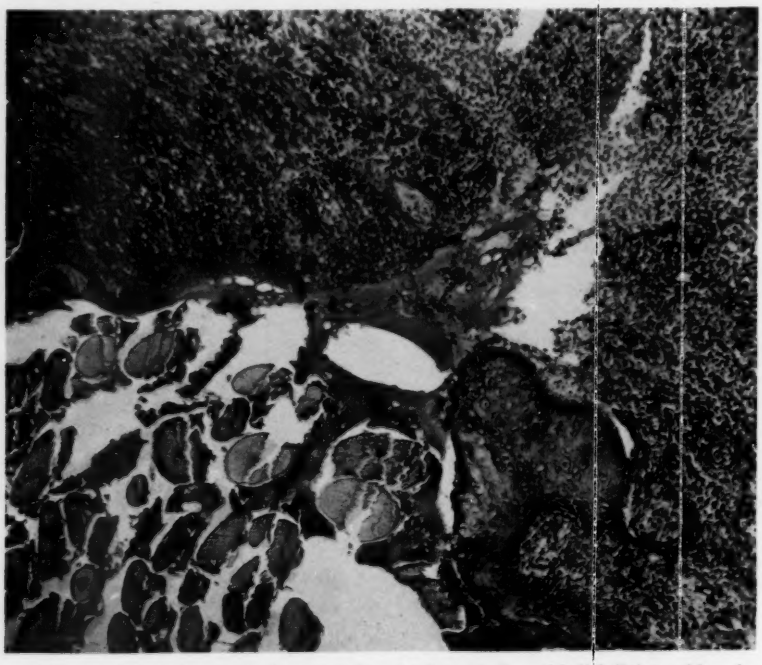

FIG. 5.—Photomicrograph demonstrating the loss of the epithelial lining with submembranous acute and chronic inflammatory reaction. Granulation tissue formation is also prominent.

The four signs are: (1) Single or multiple sinus openings in the sacrococcygeal area. They vary in number from one to five, exclusive of the secondary sinus openings; however, in rare instances sinus openings are absent. When the last condition exists, there is a small palpable tumor with a small bluish area (pin point in size) in the overlying skin. This small pin point opening can be punctured easily and a probe introduced into the underlying sinus or cyst. (2) Immature hairs may or may not protrude from the mouth of the sinus. (3) A discharge may be present which keeps the median raphé moist or soils the underclothing. (4) In rare cases cerebral spinal fluid may drip from the sinus opening. Cases portraying the latter phenomena have been reported by Moise,[4] and Ripley and Thompson.[5]

The sacrococcygeal dimple is characterized by a dimpling of the integu-

ment at the site of the sacrococcygeal junction. It is of common occurrence and practically never contains hair (bald spot of Oehlecker). The dimple is saucer-shaped and is very superficial and causes the patient no discomfort. However, if the simple dimple has been converted into a sacrococcygeal dimple sinus, the same signs occur as in the true pilonidal sinus except there is no hair protruding from the mouth of the sinus which is larger than the mouth of the true pilonidal sinus.

The direction of the pilonidal sinus is cephalad, whereas the direction of the sacrococcygeal dimple sinus is always caudad. The latter is frequently misinterpreted as a sinus of the fistula-in-ano type.

The most common complication of pilonidal and sacrococcygeal dimple sinuses is infection with abscess formation which is very painful because of its location. The abscess in the majority of instances occurs on either side of the midline, seldom involving the sinus or its cystic dilatations directly, except when the cystic dilatations are just beneath the overlying skin. In the latter condition, which is not common, an abscess usually develops in the cyst. The clinical symptoms are those of an acute infection, both locally and systemically. However, the local manifestations are severe as compared to the systemic reactions, which are very mild. The abscess usually ruptures spontaneously or is incised surgically, both of which result in the formation of accessory sinuses. The author observed one patient with 27 accessory sinus openings, who still harbored his undisturbed pilonidal sinus. When the abscess is confined to a superficial cyst and ruptures or is incised, a typical granuloma results (Fig. 2). The most formidable (fortunately rare) complication that can occur is the discharge of cerebral spinal fluid from the sinus. It is always of serious import, because if secondary infection occurs within the sinus, or associated with it, meningitis invariably follows. Secondary meningitis in the majority of instances is caused by the Staphylococcus or Streptococcus and usually results in the death of the patient.

The diagnosis of pilonidal sinus and "sacrococcygeal dimple sinus" is so simple that it is frequently overlooked. The presence of sinus openings in the midline of the sacrococcygeal region immediately establishes the diagnosis of pilonidal sinus. If every patient who consults a physician could have the sacrococcygeal region routinely examined the percentage of incidence would be greatly increased. It is only by this method of examination that uncomplicated cases of pilonidal sinus can be diagnosed and operated upon before infection occurs. In all patients complaining of a discharge, pain, or discomfort in the sacrococcygeal or anal region the likelihood of a pilonidal sinus being responsible for the clinical symptoms must be considered. In all patients who have sacrogluteal sinuses or granulomata, the nates should be separated and a pilonidal sinus will usually be discovered.

The presence of an abscess in the sacrococcygeal area in the midline or on either side of the midline is indicative of a pilonidal sinus. It is, however, common for the attending physician to incise the abscess, treat it over a period of weeks, and then wonder why the sinus persists. He frequently does not

look for the pilonidal sinus. The patient then develops a secondary sinus which is likely to result in recurrent abscess formations. One patient mentioned above had 27 abscesses incised which resulted in as many sinuses. The patient still retained his pilonidal sinus.

The only difficult diagnostic problem is to determine the extent and direction of both the primary and secondary sinus tracts. The direction can be determined by simply introducing a probe into the sinus tract and noting the direction as the probe follows the sinus tract. The extent of the tract and the presence of cystic dilatation and accessory pockets can only be determined preoperatively by injecting the sinus with an opaque substance, preferably lipiodol. The sinus is then radiographed with the patient in the prone and lateral positions. The anteroposterior position determines the size and lateral projection, and the lateral position determines the extent of the sinus. The latter method is the only way by which a sinus in the sacral canal can be diagnosed.

Treatment.—The ideal treatment of pilonidal sinus is complete surgical extirpation and primary closure of the wound. Whether this can be accomplished or not is dependent upon the presence or absence of an acute infection in or associated with the pilonidal sinus or cyst. In the presence of an acute abscess within the sinus or cyst or in juxtaposition with the deep-seated cyst, the surgical requirements are simple incision and drainage. The infection should then be actively treated until the acute manifestations have subsided. Radical extirpation of the sinus should be deferred for at least six months. In the interim the chronic infection resulting from the acute process should be minimized as completely as possible by adequate treatment of both the infected cyst and accessory sinuses. This allows the surrounding tissue an opportunity to develop a local immunity which will inhibit to a greater or lesser degree secondary infection at the time of surgical extirpation. In patients with a history of previous infection, who present at the time of their first examination multiple accessory sinuses, operation should be deferred for a week or ten days. This allows time for energetic treatment of the sinuses. The treatment consists of hot tub baths and hot moist compresses of hypertonic saline solution to the diseased area. This procedure is very important as a preoperative measure in preparing the field for operation, reduces exudation and minimizes infection following operation. No patient having secondary sinus infection subsequent to abscess formation should be operated upon without the above plan of preoperative preparation. If the above principles are adhered to, then accessory sinuses and granuloma formation are not contraindications to successful extirpation and primary closure of the wound.

The high incidence of recurrence following operation for the cure of pilonidal sinus varies greatly in different clinics. In some of the clinics the incidence of recurrence is very high, while in others very low. However, in all series reported there have been recurrences. The percentage of recurrences in the series reported by Kleckner[6] is probably the lowest. He

reports a collected series of 4,699 cases with an incidence of recurrence of 2.9 per cent. In analyzing this extensive series, he divides them into the following groups: In 4,231, the open method was used (total excision of the primary and secondary sinuses, wound packed and allowed to heal by granulation) with a recurrence in 48 cases, or 1.13 per cent; in 365 cases, total excision with primary closure of the wound with a recurrence of 33.29 per cent. In the third group there were 103 cases, with primary closure of the wound; however, due to secondary infections the wounds were opened for drainage and then allowed to heal by granulation. In this series there was an incidence of recurrence of 4.8 per cent. It is remarkable that there should be so high an incidence of recurrence of pilonidal sinus with total excision and primary closure of the wound, and a very low incidence of

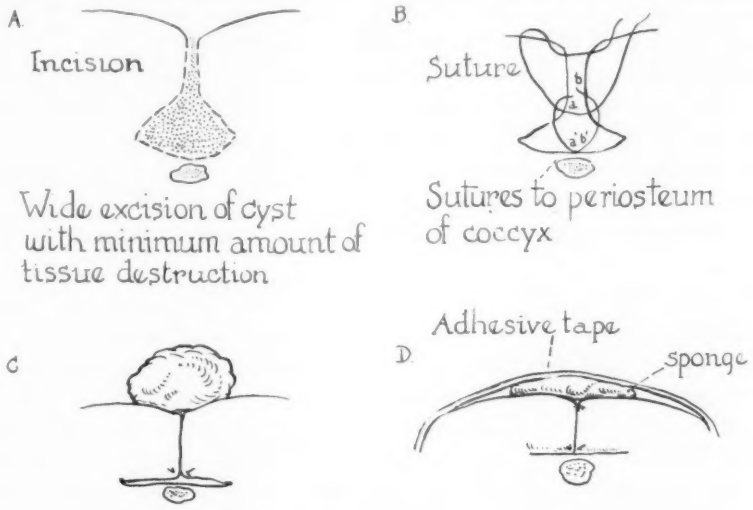

FIG. 6.—Drawing (exaggerated) illustrating the defect, following the removal of a pilonidal sinus (A); the sutures used to close the defect (B); subcutaneous defect after suturing (C); and the obliteration of all dead space and approximation of all wound surfaces by "sea sponge" pressure (D).

recurrence following excision and packing the wound, allowing it to heal by open granulation. The question that immediately confronts one is, why is there such a marked difference in the incidence of recurrence in the two methods of treatment? The incidence of recurrence is dependent upon several factors which are controllable by the surgeon, which if controlled will eliminate the recurrences.

One of the most important factors responsible for recurrence is the presence of infection in both the primary sinuses and cysts as well as the secondary sinuses. When secondary sinuses are present infection is not only present but the sinus tract is partly or completely lined by epithelium. In the majority of instances the sinuses are filled with granulation tissue, with acute or subacute and chronic infection present. If the infected primary and

secondary sinuses are thoroughly treated and stained preoperatively, the entire pilonidal sinus, its cystic dilatations and secondary sinuses, can be removed safely, the wound closed by primary suture, with complete healing resulting.

The second factor and the one which is most important is the failure to obliterate dead space at the time of primary suture of the wound. After removal of the pilonidal sinus and especially those complicated by accessory sinuses, there remains a relatively large subcutaneous defect which cannot be obliterated by sutures (Fig. 6). This leaves a dead space which becomes infected, granulation tissue is formed, and extensive scar tissue results. There results a cavity filled with infected granulation tissue surrounded by a wall of scar tissue. A sinus to the exterior is formed and with a persistence of symptoms or a recurrence. If this subcutaneous defect which cannot be closed with sutures could be completely obliterated and the obliteration maintained, recurrences would not occur. The subcutaneous defect or dead space can be obliterated easily and so maintained until complete healing has resulted by the simple means of sea sponge pressure. This method of approximating wound surfaces which obliterates all dead spaces until wound healing is complete is employed extensively by plastic surgeons. Therefore, this second factor, as the first, is under direct control of the surgeon.

The third factor, but probably the one of least importance, is the failure of complete removal of the epithelial lined pilonidal sinus and its accessory sinus tracts. If one will refer to the section on pathology, it is realized that the only sinus tracts likely to be incompletely removed are those that enter the sacral canal. By injecting the sinus with lipiodol followed by roentgenographic visualization the type and extent of the sinuses can be determined accurately preoperatively. Also, if the sinus tracts are deeply stained by a solution of methylene blue preoperatively, incomplete removal should not occur. The third factor is also under the control of the surgeon. Therefore, if all three factors responsible for recurrences are controllable by the surgeon, there should be a method by which complete surgical excision and primary wound closure could be accomplished, resulting in a high percentage of complete cures and a negligible incidence of recurrences.

Preoperative Preparation.—The method used in our clinic that controls all of the above factors, which has been described elsewhere,[1] is as follows: When the patient is first seen he is examined for the presence of infection in the pilonidal sinus. If infection is present either in the primary sinus or secondary sinus or both, the infection is vigorously treated until the infecting organisms have been sufficiently reduced to justify surgical excision. No instrumentation or injection should be undertaken until all infection has subsided. Then the sinus is probed to determine its direction and extent. This is supplemented by anterior, posterior, and lateral roentgenograms of the sacrococcygeal region following the introduction of lipiodol into the sinus and its ramifications. Having determined by the above method the type and

extent of the pilonidal sinus, the next and most important procedure is to thoroughly stain the sinus, its cystic dilatation, as well as its accessory sinuses. This staining is accomplished as follows: Five days before the operation the pilonidal sinus is injected with a solution of methylene blue under slight pressure. This injection is again repeated on the fourth and third preoperative days, respectively. Two days now elapse before the operation. This allows the sinus tract to "dry out," leaving the walls of the cyst and sinus deeply stained a bluish color. This method of staining the sinuses confines the stain to the sinus tract and prevents staining of the surrounding tissue at operation. The surgeon can easily distinguish the diseased from the normal tissue, whereas, if the sinus is injected at the time of operation, the dye solution spills into the operative field. The dye solution immediately stains

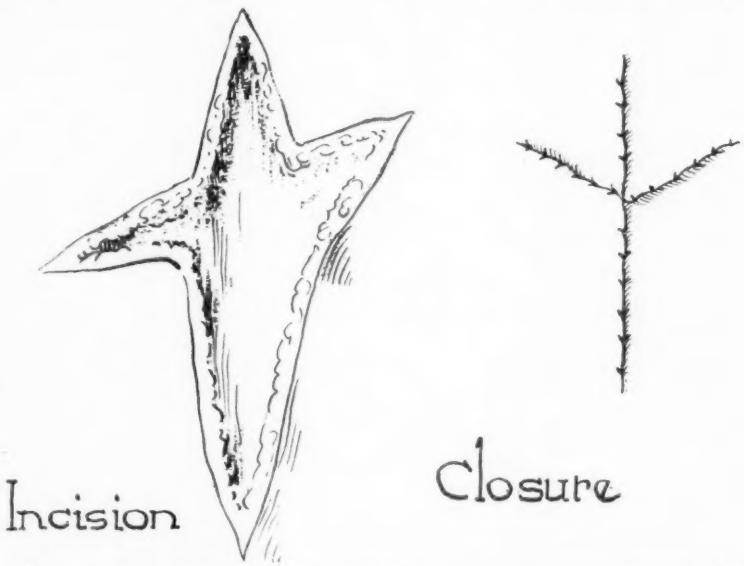

FIG. 7.—Drawing illustrating the method of excising the primary pilonidal sinus and the lateral or secondary sinuses, and the wound after closure.

all exposed tissue and the normal and abnormal are of the same color and cannot be distinguished from each other. By the above method failure to remove completely all of the sinus tract is eliminated.

Operative Procedure.—After the sinus tract has been defined and stained the operation proceeds as follows: With the patient in the prone position, a pillow is placed beneath the pubis and adhesive straps are applied to the buttocks on either side and fastened to the table. The adhesive straps separate the buttocks and act as retractors. In the noninfected type an incision can be made directly into the sinus, the sinus easily dissected from the surrounding tissue with a minimum loss of tissue, and the resulting wound can be easily closed by suture. However, in the majority of instances secondary sinuses are present and necessitate a more extensive dissection, which can be accomplished also with a minimum loss of tissue. An elliptical

incision is made around the primary sinus opening and extends down to the periosteum over the sacrum or sacrococcygeal region (Fig. 7). If necessary a probe can be easily introduced from the mouth of the accessory sinus through the tract into the open wound. This will facilitate the dissection of the secondary sinus tracts. The wound is thoroughly inspected and remnants of the sinus tract searched for. All bleeding points are now ligated with fine silk and the wound closed by retention sutures of silk or silkworm gut. After closure of the wound edges an unobliterated dead space is always present at the bottom of the wound due to the nature of the wound (Fig. 6). If this dead space is not obliterated a recurrence will take place. Therefore, complete apposition of all wound surfaces and obliteration of all dead spaces is secured by pressure over the wound. This pressure must be constant and distributed evenly, and is obtained only by the use of sea sponges (Fig. 6). This pressure dressing is left undisturbed for a period of 10 to 12 days. If, however, it becomes necessary to change the dressing, the sponge pressure must be repeated. In reapplying the sponge pressure, one should never use the same sponges, because they become molded to the parts and have lost their resiliency, having been applied while wet. Therefore, a fresh, sterile, moist sponge must always be used in redressing the wound.

The above method has been employed in 42 cases of pilonidal sinus, without a single recurrence. There have been nine cases of skin infection with good healing, and one case that developed a deep infection which necessitated wound opening. This case healed by open granulation.

Dr. L. H. Strug[7] has used the same method in 54 cases with primary healing of the wound in 52. One case had a Streptococcal gangrene of the skin, and the other had an accumulation of serum in the wound, which was aspirated three times before healing was completed. There have been no recurrences in Doctor Strug's series.

CONCLUSIONS

Pilonidal sinuses and cysts are of common occurrence. They are derived from that part of the caudal end of the medullary canal located in the tail anlage. They are divisible into four groups: (1) Sacrococcygeal dimple and sacrococcygeal dimple sinus; (2) true pilonidal sinus, confined to the subcutaneous tissue; (3) true pilonidal sinus extending into the sacral canal; and (4) true pilonidal sinuses which are continuous with the subarachnoid space and canal of the spinal cord.

A method is described by which surgical excision and primary suture will give a high percentage of cures and a low incidence of recurrence.

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GAS GANGRENE FOLLOWING THERAPEUTIC INJECTIONS

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GAS gangrene, developing as the result of subcutaneous or intramuscular medicinal injections, has been reported in the foreign literature in numerous papers, but, to date, there has appeared only one article in the American literature dealing with this condition. In 1936, Tenopyr and Shafiroff[59] reported three cases of gas gangrene following hypodermoclysis. Two of these patients died, and one recovered.

The first cases, of which the author was able to find any record, were reported by Brieger and Ehrlich,[9] in 1883. The first was that of a woman, age 26, who was extremely ill with typhoid fever. She had received a subcutaneous injection of moschus tincture into the right thigh. On the second day thereafter, typical symptoms of gas gangrene developed at the site of the injection, with swelling, pain, crepitation and discoloration. The patient died the following day without surgical intervention. The second case was that of a woman, age 32, also suffering from typhoid fever. She had received injections of ether and oil into the thigh. On the second day following the injections, the typical clinical findings of gas gangrene developed in the injected thigh, and on the fourth day the patient died without surgical intervention. The bacillus of malignant edema was found in both cases.

The second article dealing with this subject was that of Fraenkel,[16] in 1893, who reported two cases. One of these cases followed the injection of camphor, oil and ether, and the other of morphine. Other instances have been reported at irregular intervals since that time, until the later years of the World War, when the incidence of reported cases increased sharply. Seventy per cent of reported cases have appeared in the literature during the last ten years. In 1933, Junghahns[27] collected 60 cases. Twenty-five additional cases have been found in the literature, and one case of our own is added, making a total of 86 cases of gas gangrene following the injection of medicaments.

Case Report.—W. P., colored, male, age 63, was admitted to the Bryn Mawr Hospital April 3, 1936. A tentative diagnosis of partial intestinal obstruction was made at the time of admission, and during the next two days the patient received several intravenous injections of glucose in normal saline solution, into the veins of both arms. On April 5, an exploratory celiotomy was performed through a lower right rectus incision. A loop of the lower ileum was found to be strangulated in the right inguinal canal. The bowel was released, and after its viability had been determined, it was replaced in the abdomen. The internal abdominal ring was closed from within, and the abdominal wound sutured.

Postoperative Course.—Before and after operation, the patient received injections of morphia into the arm. During the afternoon and night of the third postoperative day, the

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patient received one injection of pitressin, and five injections of digalen. One of the injections of digalen was given into the right thigh. The other injections were given into the arms. Twenty-four hours after receiving the injection into the thigh, the patient complained of pain at the site of the injection. Upon examination, the thigh was swollen, tender and hot, these signs being most marked at the site of the injection. No crepitation was elicited at this time, and hot, wet dressings were applied. During the course of the next 12 hours, the patient's temperature rose from normal to 102.3° F. The local signs in the thigh became more marked, and crepitation was elicited.

Under local anesthesia, wide incisions were made into the infected thigh, and antiperfringens serum was administered, both into the tissues about the wound, and intravenously. The tissues were found to be distended with gas, and necrotic.

The patient expired six hours following this operation. Cultures of the infected tissues and of the skin of the unaffected thigh showed gram-positive rods which produced gas under anaerobic conditions. Culture of the digalen solution was sterile, but the syringe and needle were not cultured.

Seventy-six of the 86 cases reported, terminated in death, a mortality of 88.4 per cent. This figure is in marked contrast to the mortality of 49.7 per cent in 607 collected cases of gas gangrene following various injuries (Miller[40]).

The sites of injections were stated in 59 cases reported in the literature, and of these, 55 were in one or both thighs, the buttocks, or abdominal wall. Table I gives the sites of injection, and Table II shows the wide variety of drugs injected:

TABLE I

SITES OF INJECTIONS

One thigh	45
Both thighs (both injected and both infected)	3
Buttock and arm (both injected and both infected)	3
Thigh and arm (both injected and both infected)	2
Breast	2
Arm	2
Abdominal wall	1
Buttock	1

In nearly all cases reported, drugs, syringes, needles and solutions were cultured. A preparation of caffeine and digitoxin was found to contain gas organisms by Heuss.[25] Nauwerck[42] found gas bacilli in a preparation of caffeine sodium salycilate solution. Semenoff[57] and Anschutz[1] were able to culture gas bacilli from the needles used in their cases. These needles had been preserved in 96 per cent alcohol. Dimtza[12] found gas bacilli in one syringe, one needle, and in four files of the type used in breaking glass ampules. In all other instances in which studies were carried out, the drugs, solutions, syringes and needles were found to be sterile.

The patients to whom the injections were given suffered from a wide

TABLE II

MEDICAMENTS INJECTED

Caffeine	19
Adrenalin	11
Saline solution	9
Camphor	7
Quinine	5
Hackel's anti-asthmatic serum	5
Morphine	3
Digalen	3
Asthmalysin	2
Moschus tincture	2
Novocain	2
Ether and oil	2
Digatotal	1
Omnidine	1
Afenil	1
Calcium	1
Digipurate	1
Scopolamine	1

variety of diseases. Almost all of them were severely ill. The most frequent diseases were pneumonia, typhoid and malaria.

The time elapsing between the injection of the drug and the appearance of the clinical symptoms of gas gangrene was difficult to determine in most instances. This was true because the patients had usually received several injections over a period of several days. In 21 cases, we can say with certainty that clinical symptoms appeared between ten and 36 hours following the contaminated injections.

The time elapsing between the appearance of the clinical symptoms and the time of death could be accurately determined in 45 cases (Table III).

TABLE III

INTERVAL BETWEEN APPEARANCE OF CLINICAL SYMPTOMS AND DEATH

17 died during the first day
21 died during the second day
3 died during the third day
1 died during the fourth day
2 died during the sixth day
1 died during the seventh day

No attempt has been made in this paper to deal with the bacteriology, clinical course or treatment of gas gangrene. Attention is drawn to the facts that gas gangrene can and does occur after the hypodermic or intramuscular injection of medicinal agents; that the mortality is very high; *i.e.*, above 88 per cent, and that injections in the thigh are much more likely to be followed by gas gangrene than injections elsewhere in the body. The relatively high mortality in the cases in this series is possibly due to the fact

that almost all of the patients were severely ill before the contaminated injections were given. It is considered highly significant that 55 out of 59 contaminated injections were given into areas of the body surface which might easily be soiled by fecal material. For this reason, it is recommended that such areas—namely, the thighs, buttocks, and abdominal wall—be avoided when giving hypodermic or intramuscular injections. If these areas must be used, then the skin should be carefully sterilized, instead of receiving the perfunctory dab with an alcohol sponge, which is customary in most hospitals.

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THE EFFECT OF CONSTANT GASTRIC SUCTION ON THE ACID-BASE EQUILIBRIUM OF THE BODY*

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WESTERMAN,[1] in 1910, introduced and popularized the use of the stomach tube for the postoperative treatment of peritonitis. This discovery was as far reaching in its effects and its benefits to the surgical patient as the stethoscope has been to the medical patient. Levine,[2] in 1921, introduced his duodenal catheter which was a great improvement over the instrument of Westerman, especially so in its ease of application and usefulness. In 1925,[3] Ward[4] first presented an apparatus for producing constant gastric suction, and, in 1930, described remarkably beneficial results with the use of this instrument in acute dilatation of the stomach. He also advocated its use in paralytic ileus, intestinal obstruction, and postoperative vomiting. Many modifications of Ward's apparatus were described during the following years,[5, 6, 7, 8] the principal one of which was that of Wangensteen,[9, 10, 11, 12, 13, 14] first described completely in 1933, and which immediately became universally employed.

The Wangensteen apparatus (Fig. 1) has been used in the State of Wisconsin General Hospital since its first description in 1933 to the present time, with minor modifications. It consists essentially of a closed system containing water which creates a constant negative pressure on an inlying Levine duodenal tube. The use of this apparatus postoperatively has reduced the mortality and morbidity of all patients in whom upper abdominal surgery has been performed. It has also been life saving in cases of intestinal obstruction when used alone, or in conjunction with operative measures. Many authors[15] consider this to be the greatest advance in the care of surgical patients recorded during the past decade.

During the past two years, some disadvantages of the employment of constant gastric suction have been noted. Taylor[16] has reported two cases of alkalosis, resulting in death in one instance, following its use.

The Acid-Base Equilibrium of the Body.—This is a finely balanced mechanism which remains remarkably constant unless seriously interfered with. Gamble's[17] description of this mechanism, in 1924, is probably the best and most readily understood outline of this difficult subject. He considered the important basic constituent of all body fluids to be sodium and the important acid constituents of all body fluids to be the chlorides and carbonic acid.

* Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfillment of the requirements for the degree of Master of Medical Science (M.Sc.[Med.]) for graduate work in surgery. Submitted for publication May 4, 1938.

Figure 2 graphically depicts Gamble's concept of this equilibrium. He also showed that a loss of the sodium ion from the body is the essential factor in rapid dehydration, and that vomiting causes more of a loss of the chloride ion than of the sodium ion; therefore, alkalosis ensues; the coincidental loss of

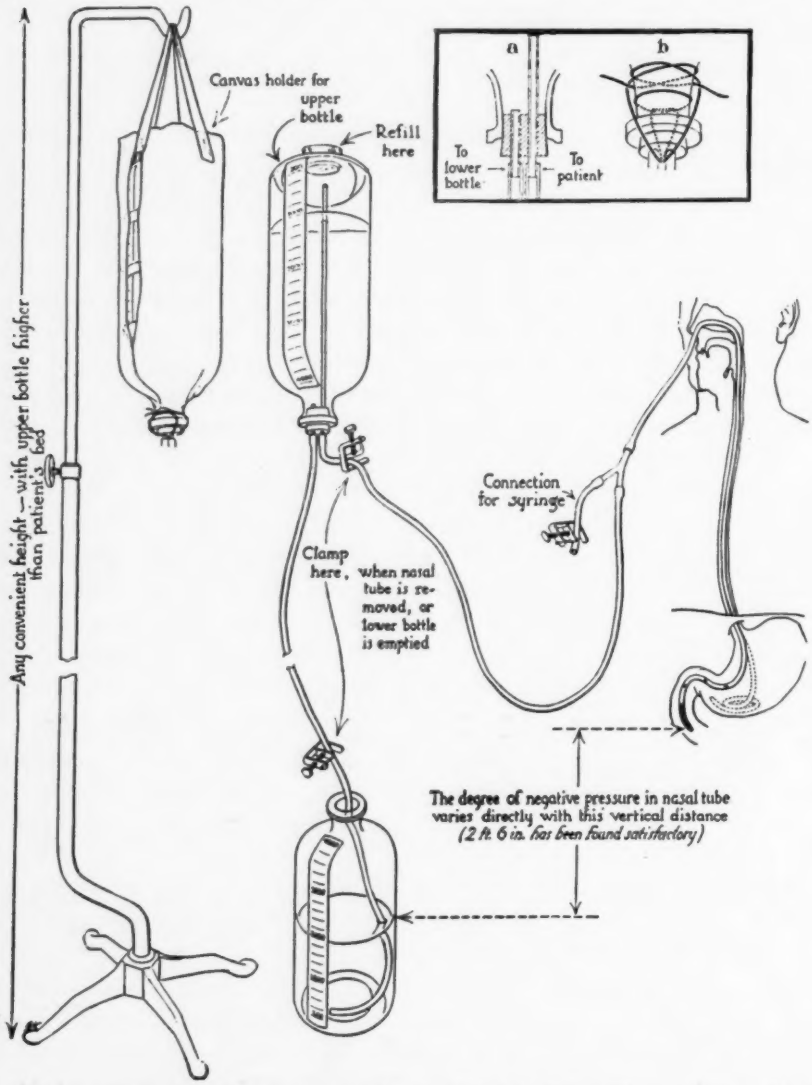


FIG. 1.—Illustrating the apparatus, as originally devised by Doctor Wangensteen,[9] employed to effect continuous gastric or duodenal suction. (Reproduced from Minn. Med., 16, 96, 1933.)

sodium, however, causes the dehydration. Alkalosis was reduced somewhat by an increase in carbonic acid to balance the loss of chlorides. With the kidneys in good condition and functioning normally, a moderate increase of either an acid or an alkali radical will be compensated for by having the excess

excreted in the urine; and, in the case of carbonic acid, the lungs aid in its excretion as carbon dioxide.

Method of Determination.—The best means of estimating the relative acid or basic properties of the human organism are by blood determinations of the carbon dioxide combining power and the blood chloride. The CO_2 combining power is considered normal anywhere between 40 and 60 volumes per cent, and chloride values are considered normal between 400 and 600 mg. per 100 cc.

Chemical Changes Produced by Depletion of Gastric Juice.—These have been studied by MacCallum and coworkers,[18] Hadon and Orr,[19] Gamble and Ross,[17] Dragstedt and Ellis,[20] and Hastings *et al.*[21] They all agree that the continued loss of gastric juice leads to dehydration, alkalosis and death, and have produced experimental evidence to support those views. There are, however, no data available showing the chemical changes produced in the blood by the clinical application of the Wangensteen apparatus.

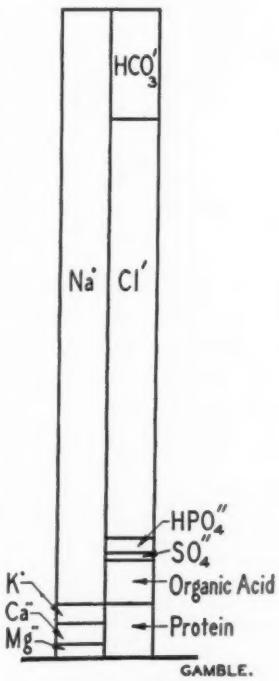


FIG. 2.—Graphic representation of Gamble's[17] concept of the acid-base equilibrium of the body. (Reproduced from J. Clin. Investig., 1, 403, 1924–1925.)

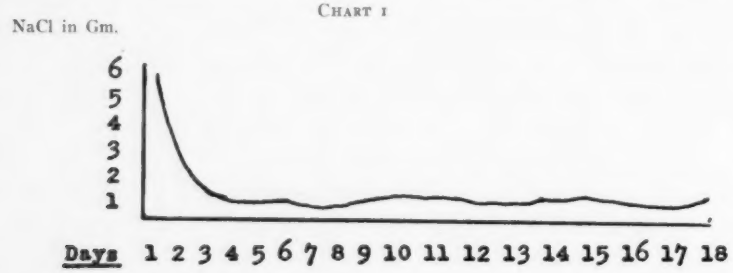
For purposes of this study, 50 ward cases, in which the Wangensteen apparatus was employed, were followed. These cases were chosen at random and included, for the most part, patients who had had upper abdominal surgery performed or who were suffering from some form of intestinal obstruction, either pre- or postoperatively. Daily estimations were made of the blood chlorides and CO_2 combining power. The intake and output of all fluids, both oral and parenteral, were recorded, and the quantitative estimation of chlorides removed by the gastric suction determined. Retention tests were also performed daily, to determine whether or not the obstruction in the gastro-intestinal tract, due either to operative trauma with edema or an actual obstruction, had become patent and was permitting some of the gastric juice to pass into the intestines.

Results.—In the present investigation it was found that from one to four liters of fluid could be removed daily from the stomach by the Wangensteen apparatus and, along with this, one to 14 Gm. of chlorides. The amount of chlorides removed had no relationship to the acidity of the stomach, regardless of whether a hyperchlorhydria or an achlorhydria was present previously. This agrees with the observations of Cohen,[22] the result of animal experimentation. The administration of large quantities of fluid orally, producing a lavage action on the stomach, was the principal factor in causing an increase in gastric secretion, in both our observations and in those of others.[9, 16] The amount of

parenteral fluids, especially so in the case of saline solution, also played a prominent rôle.[20]

Chart 1 represents a composite graph of the chloride loss in the usual postoperative cases in which the Wangensteen apparatus was used for only a few days. The gastric tube in this type of case was removed as soon as it could be demonstrated, by a retention test,* that the pyloric or operative stoma had become patent, was functioning, and permitted gastric juice to pass

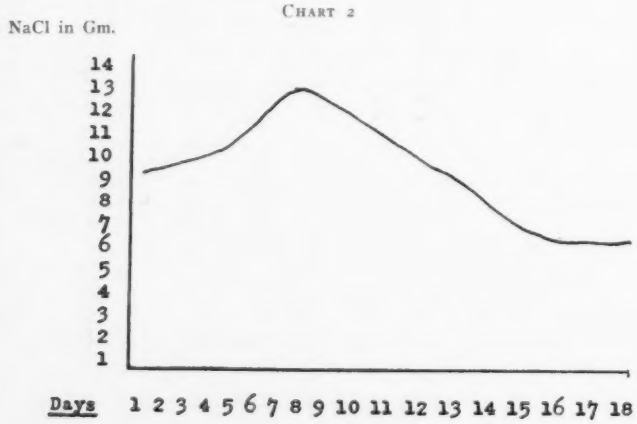
CHART 1



Average secretion of NaCl following operation and application of constant gastric suction.

into the intestines. It will be noted that, on the first day postoperatively, about 6 Gm. of chlorides were removed by the suction apparatus, and this rapidly tapered down to 1 Gm., coincident with the opening of the pyloric or operative stoma, as soon as the edema resulting from the operative trauma had subsided, which allowed some of the chlorides in the stomach to pass into the intestines.

CHART 2



Cases in which stoma does not open.

Chart 2 represents a composite graph of the chloride loss of those cases in which the stoma failed to open in the usual time. In these cases the chlorides

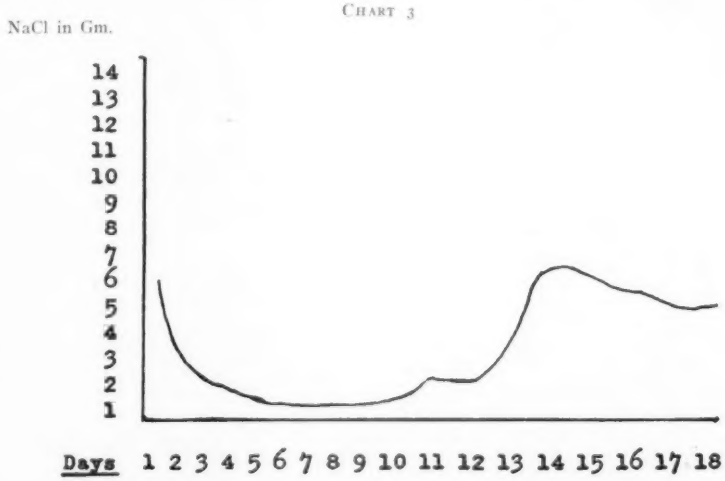
* A retention test is performed by emptying the stomach through the inlying gastric tube and then placing 200 cc. of water into the stomach and clamping off the tube. At the end of two hours the water remaining in the stomach is siphoned off and measured. If the amount obtained is less than 30 cc., this indicates to us that the pyloric or operative stoma is open and material from the stomach is passing into the intestines.

were lost in the amount of 6 to 14 Gm. daily, and had to be supplied parenterally to prevent changes occurring in the chemical balance of the blood.

Chart 3 represents a composite graph of the chloride loss of those cases in which the stoma opens for a time and closes later because of a breakdown of the anastomosis, or obstruction due to infection, adhesions, *etc.* In this instance the usual drop and leveling off of the curve occurs, to be followed later, when the obstruction intervenes, by a rapid rise.

Numerous other factors that influence the amount of chlorides lost were also appreciated. As previously mentioned, the amount of fluids given orally and parenterally was the most important factor in causing an increase in chloride secretion in the stomach, as determined by their subsequent removal

CHART 3



Cases in which stoma opens after operation and then closes later.

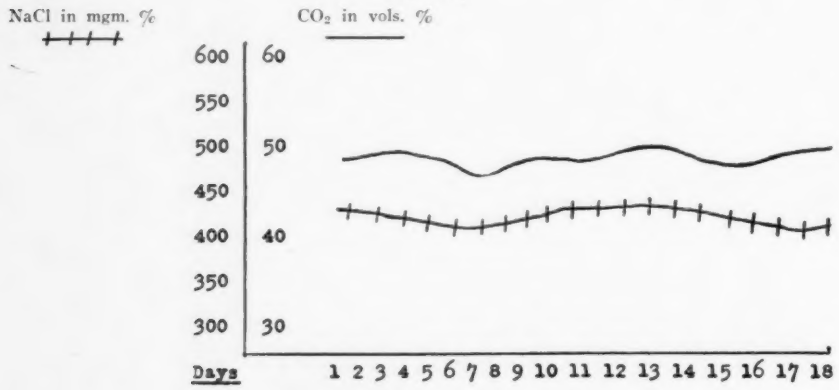
by the Wangensteen apparatus. Psychic stimulation also seemed to play a minor rôle, as did also drug therapy. When large sections of the stomach were resected, the chloride secretion was always found to be somewhat lessened in these cases. The development of peritonitis, pneumonia, or starvation, all of which have a tendency to produce acidosis, slowed down the loss of chlorides and consequent tendency toward alkalosis.

The blood changes in our clinical cases, followed by CO_2 and chloride estimations, were unusually constant and within normal limits. Even though parenteral saline solution was withheld from several patients for periods of four days to one week, no significant change in their blood chemistry occurred. This would seem to indicate that, as long as minimal amounts of gastric juice are able to pass into the intestines and be absorbed, the acid-base equilibrium will be maintained and that, in the presence of a complete block at the operative or pyloric stoma, the body stores of chlorides could be expected to prevent any changes in the blood chemistry for several days. We did not have the courage to permit any of our cases to develop alkalosis, by withholding parenteral administration of saline solution for a sufficiently long period, as it

was considered that this phenomenon could be adequately demonstrated by animal experimentation. However, the two cases reported by Taylor and several personal communications from other observers are ample evidence of what may, and will, take place from too great a loss of chlorides. Chart 4 represents a composite graph of the blood changes encountered in our cases.

In animal experimentation on dogs, we created gastric fistulae, to study the effect of the loss of chlorides on their acid-base equilibrium, as the nearest approach to what we were dealing with clinically. This was only corroborative of the observations of previous workers.[17, 18, 19, 20, 21] We did, however, find that alkalosis could be produced only by the total loss of gastric secretion and

CHART 4



Blood changes in clinical cases.

that, if the pylorus were not tied off or blocked artificially, the changes produced in the blood chemistry would be insignificant. These findings have worked in very nicely with the observations on the opening and closing of the stoma in our clinical cases with the subsequent loss of minimal or very great amounts of chlorides.

In one dog, we created a gastric fistula and followed his blood changes for 22 days, without noting any marked deviations. A second operation was then performed in which the pyloric sphincter was tied off and within a few days the chlorides dropped to values around 100 and the CO_2 rose to values over 100, with the production of alkalosis and death. No saline solution was administered parenterally to combat this.

The patients showed no edema following the administration of moderate amounts of saline solution, but in several of the experimental animals, to which we administered huge amounts of saline solution, this phenomenon was noted. Coonse[23] and others[24] have previously noted this effect. These observers attribute the edema to elevation of the blood chlorides and postulate that, when patients with kidney insufficiency are given doses of sodium chloride of 15 to 20 Gm. daily, edema will occur. Helwig,[25] *et al.*, report a case in which an overzealous nurse administered nine liters of tap water in 24 hours, by proctoclysis, causing the death of the patient soon after in convulsions.

Two of our cases, that had had an indwelling gastric tube for more than ten days, came to autopsy, and, on examination, showed a moderate amount of ulceration of the nasopharynx and esophagus in each. These changes were unquestionably due to a pressure necrosis from the gastric tube.

CONCLUSIONS

(1) The Wangensteen apparatus is a definite aid in the postoperative treatment of many patients, but has certain limitations and dangers.

(2) The production of alkalosis and death by constant gastric suction, used under ordinary circumstances, is almost impossible to attain unless there is a complete obstruction at the pylorus, or operative stoma.

(3) With obstruction at the pylorus or operative stoma, alkalosis will be produced within five to eight days, unless sufficient parenteral saline solution is administered to combat it.

(4) Excessive amount of saline solution, administered parenterally, will produce edema of the tissues, especially so in the presence of damaged kidneys.

(5) Cases requiring constant gastric suction for periods extending over ten days are apt to develop necrosis and ulceration of the nasopharynx and esophagus.

Acknowledgment and appreciation is made of the help and constructive criticism of Dr. Erwin R. Schmidt in the preparation of this paper and also the assistance of Dr. Marion Kimble in making the necessary chemical analyses.

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MEMOIR

FREDERIC JAY COTTON

1869–1938

In the death of Dr. Frederic J. Cotton the surgical profession of America lost a member of great and varied talents, industry, and ability who had greatly impressed his personality upon the surgical world, and had taken his place among the leaders of our profession.

He was born September 24, 1869, the son of Joseph P. and Isabella C. Cotton. His father was a civil engineer, and in his office he may have developed that remarkable talent for drawing that stood him in such good stead during his professional career.

He was educated at the Rogers High School in Newport, Rhode Island, was graduated from Harvard College in 1890, and from the Harvard Medical School in 1894, receiving the degree of A.M. at the same time as the M.D. degree. The A.M. degree was at that time given to graduates of the medical school who ranked high in the newly begun four-year course. He then studied bacteriology in New York and spent two years in Vienna, where, in addition to a thorough knowledge of bacteriology, he required a knowledge of French and German which later aided him greatly in his earlier years in Boston, where he collaborated in Bradford's and Lovett's book on Orthopedic Surgery. He established the laboratory of bacteriology at the Infants Hospital, and did pioneer work in the same subject at the Massachusetts General and the Children's Hospitals. He served as surgeon in the Spanish War, and his knowledge of bacteriology and of civil engineering both contributed to make his work in sanitation especially efficient.

He served for four years on the staff of the Children's Hospital during the early years of its organization, but on his resignation in 1902, was appointed surgeon to outpatients at the City Hospital where he served for 30 years, rising through all the grades to be Surgeon-in-Chief and President of the staff in 1891, when he reached the age limit and resigned. His training at the Children's Hospital had given him special interest in diseases and injuries of the bones and joints, in which subject there is a tremendous opportunity for study at the City Hospital where the street accidents of a great city are collected under one roof. He distinguished himself in the treatment of fractures and dislocations. He had named for him Cotton's fracture of the ankle (Pott's fracture with backward dislocation of the lower fragment) which he minutely described and for which he devised an effective treatment. He was particularly active in the study and treatment of fractures of the neck of the femur, which he managed by employing his own method of impaction with a mallet, and immobilization with plaster in an abducted position. He devised and practiced many ingenious methods to aid in the treatment of fractures and dislocations. As the work of the hospital expanded it was found necessary to organize a special bone and joint service. This was perfected by Doctor

Cotton. He was made chief of the service and held this position as long as he was connected with the hospital. He was for four years, from 1908 to 1912, Chief Surgeon at the Beth Israel Hospital, and Professor of Surgery in the Tufts Medical School. He was always interested in teaching, particularly graduate teaching, and was for a time Assistant in Surgery at the Harvard Medical School and afterward Lecturer in the Graduate School. He acted as consultant to many hospitals throughout New England. For several years he served as chairman of the Medical Advisory Committee of the Massachusetts Industrial Accident Board. He was clear and impressive in his language and therefore an excellent teacher, so that his ingenious and clever methods became widely known and used by the profession.

He contributed very extensively to the literature on fractures and dislocations, collaborating, as has been noted, in Bradford's and Lovett's book on Orthopedic Surgery, and Scudder's Treatment of Fractures. In 1910, his own book, Dislocations and Joint Fractures, was published by W. B. Saunders and Co. This proved very popular, and a second revised edition was published in 1924. His ability as an artist greatly enhanced the clarity and charm of his surgical writings. He wrote the division on Fractures in Lewis' System of Surgery.

He was one of the Founders of the American College of Surgeons, was a member of its first Board of Regents, and for many years served as a member of the Committee on Fractures. He served on the Board of Governors from 1925 to 1938, and at the same time was a member of the Committee on Industrial Medicine and Traumatic Surgery. For several years he served as chairman of the Massachusetts Credentials Committee. He had been selected by the Fracture Committee to give the Fracture Oration at the New York Meeting of the College in 1938. He was a member of the American Surgical Association, the New England Surgical Society, the Boston Surgical Society, the American Academy of Orthopedic Surgeons, the American Medical Association, the Massachusetts Medical Society and the Boston Orthopedic Club, of which he was at one time president.

In 1917, Doctor Cotton enlisted in the United States Army and served with distinction with the rank of Major. Previous to this he was a member of the General Medical Board of the Council of National Defence, under the chairmanship of Dr. Franklin H. Martin. He was active in reconstruction work both during and after the war, and led in the organization of the Parker Hill Hospital, of which he was Surgeon in Charge. In the summer of 1918, he was Surgeon-in-Chief at the Walter Reed Hospital. He was later Consultant to the Public Health Service and the Veterans' Bureau. Doctor Cotton was a regular attendant at medical meetings. His discussions were clear and accurate, and generally contributed something to the subject, and were illustrated by drawings on the blackboard. His many papers were original in material and clear in presentation. He was a natural teacher, and became the friend and advisor of many younger men, who regarded him as their authority on surgery of the bones and joints.

Doctor Cotton was married to Jane Baldwin of Maryland, who survives him, with a daughter, Jean, and two grandchildren.

He was an enthusiastic sportsman and made regular trips to Canadian waters in successful search for trout and salmon. His chief hobby was sculpture, and his bronzes were really excellent enough to put him in the very first rank among amateurs. He was influential in founding the "hobby exhibit" for the members of the Massachusetts Medical Society, certainly an incitement to the better use of leisure.

He had a long, active and varied career, and filled an important place in many departments of our profession. He was active in his work up to the very day of his death at his home in Boston on April 14, 1938, and so was spared a lingering illness and inactivity. He will be missed by many friends, and his loss will be felt by the entire profession.

FRED B. LUND.

TO THE EDITORS OF THE ANNALS OF SURGERY

A FEW days ago I received a letter from Dr. Alfred J. Brown of Omaha, Nebraska, enclosing a reprint entitled The Treatment of Colles' Fracture Considered from the Standpoint of Muscle Physiology, from the American Journal of Surgery of May, 1917, 21 years ago.

The method of reduction that he employed was different from the one I described in the ANNALS OF SURGERY for July, 1938. His conclusions followed a study of muscle pull while mine were reached after analyzing the results of treatment in 125 cases. In both instances complete supination seemed to be the logical position for immobilization. Figure 8 in his reprint also shows the wrist flexed and in ulnar adduction although the flexion is not mentioned in the body of the paper. His letter speaks of "Supination, slight flexion and ulnar adduction."

I wish to give to Doctor Brown the credit for priority in advocating supination (unless someone else can trace it back to Hippocrates), for Buxton's paper was published in 1926, five years later.

I studied the abstracts of 150 articles on Colles' fracture that had been prepared at my request but failed to see this splendid paper by Doctor Brown. I hope that you will publish this letter in the ANNALS OF SURGERY and that this added publicity may further stimulate the use of this better method for immobilizing Colles' fracture.

HENRY F. GRAHAM.

December 13, 1938.

ERRATA

In the Book Review of Thoracic Surgery, appearing in the ANNALS OF SURGERY, **109**, 159–160, January, 1939, Dr. Sauerbruch's name was misspelled and the publishers were "Baltimore, Wm. Wood and Company", and not Philadelphia, J. B. Lippincott Company. The title should therefore read:

BOOK REVIEW

THORACIC SURGERY. By Ferdinand Sauerbruch, M.D., and Laurence O'Shaughnessy, M.D., F.R.C.S. A William Wood Book by the Williams & Wilkins Company, Baltimore, 1938.

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